Connecting via Winsock to STN

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LOGINID:ssspta1626gms

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN
NEWS 21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS 22	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 23	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 24	May 27	Explore APOLLIT with free connect time in June 2004

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:43:32 ON 15 JUN 2004

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:44:05 ON 15 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JUN 2004 HIGHEST RN 693217-50-4
DICTIONARY FILE UPDATES: 14 JUN 2004 HIGHEST RN 693217-50-4

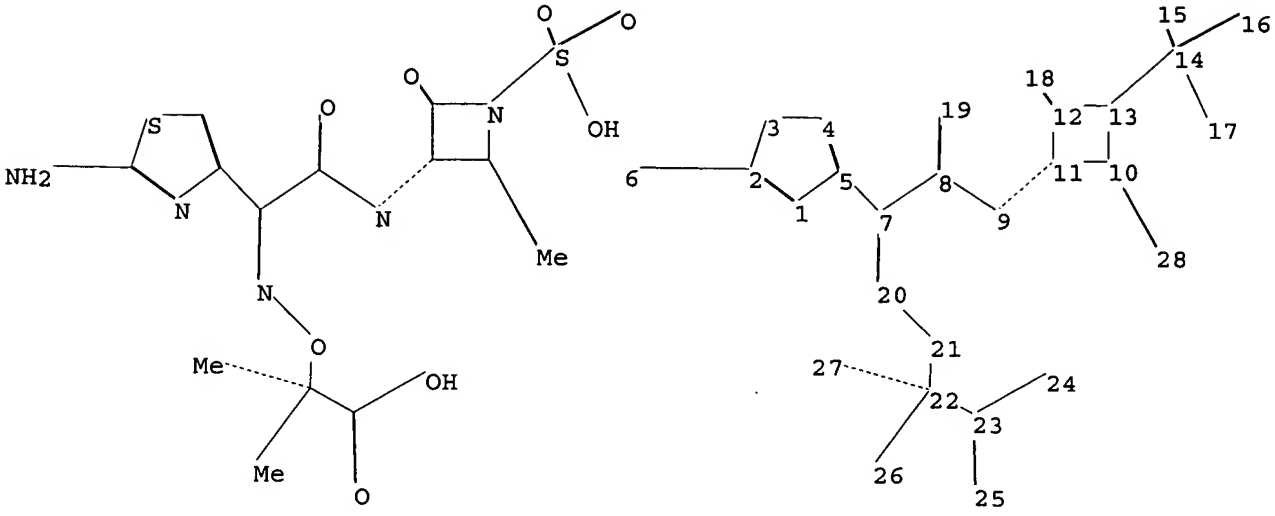
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10635659.str



chain nodes :
6 7 8 9 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
ring nodes :
1 2 3 4 5 10 11 12 13
chain bonds :
2-6 5-7 7-8 7-20 8-9 8-19 9-11 10-28 12-18 13-14 14-15 14-16 14-17
20-21 21-22 22-23 22-26 22-27 23-24 23-25
ring bonds :
1-2 1-5 2-3 3-4 4-5 10-11 10-13 11-12 12-13
exact/norm bonds :
1-2 1-5 2-6 7-20 8-9 8-19 9-11 10-11 10-13 11-12 12-13 12-18 13-14
20-21 21-22 22-27
exact bonds :
2-3 3-4 4-5 5-7 7-8 10-28 22-23 22-26
normalized bonds :
14-15 14-16 14-17 23-24 23-25
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS

Stereo Bonds:

28-10 (Single Wedge).

Stereo Chiral Centers:

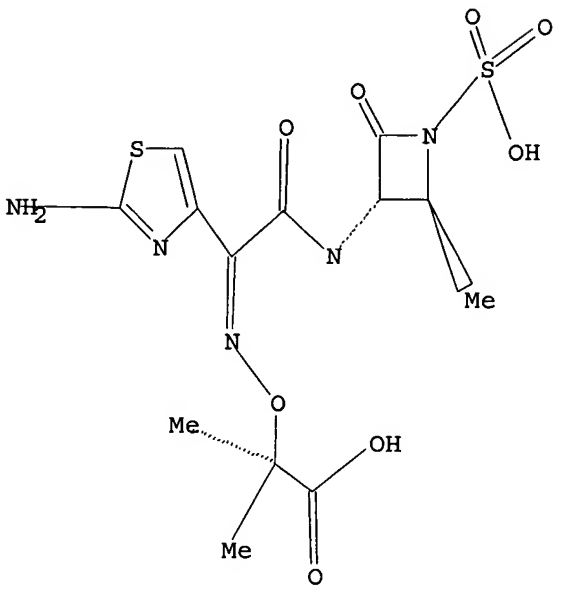
10 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 10

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:44:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 36 TO ITERATE

100.0% PROCESSED 36 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 360 TO 1080
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:44:32 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 683 TO ITERATE

100.0% PROCESSED 683 ITERATIONS 67 ANSWERS
SEARCH TIME: 00.00.01

L3 67 SEA SSS FUL L1

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 155.42 155.63

FILE 'CAPLUS' ENTERED AT 11:44:45 ON 15 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 15 Jun 2004 VOL 140 ISS 25
FILE LAST UPDATED: 14 Jun 2004 (20040614/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3
L4          1926 L3
=> s l3/p
L5            33 L3/P

=> s l5 and acid
        3829624 ACID
        1435155 ACIDS
        4296917 ACID
                  (ACID OR ACIDS)
L6            25 L5 AND ACID

=> s l5 and mineral(w)acid
         328366 MINERAL
         226487 MINERALS
         459376 MINERAL
                  (MINERAL OR MINERALS)
        3829624 ACID
        1435155 ACIDS
        4296917 ACID
                  (ACID OR ACIDS)
          18379 MINERAL(W)ACID
L7            2 L5 AND MINERAL(W)ACID

=> s l5 and aqueous(w)acid
         157948 AQUEOUS
              1 AQUEOUSES
         157949 AQUEOUS
                  (AQUEOUS OR AQUEOUSES)
         989182 AQ
            145 AQS
         989268 AQ
                  (AQ OR AQS)
        1021249 AQUEOUS
                  (AQUEOUS OR AQ)
        3829624 ACID
```

```
       1435155 ACIDS
       4296917 ACID
                 (ACID OR ACIDS)
          7241 AQUEOUS(W)ACID
L8           1 L5 AND AQUEOUS(W)ACID

=> d his

     (FILE 'HOME' ENTERED AT 11:43:32 ON 15 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 11:44:05 ON 15 JUN 2004
L1               STRUCTURE UPLOADED
L2             5 S L1
L3            67 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 11:44:45 ON 15 JUN 2004
L4          1926 S L3
L5            33 S L3/P
L6            25 S L5 AND ACID
L7             2 S L5 AND MINERAL(W)ACID
L8             1 S L5 AND AQUEOUS(W)ACID

=> s l6 and p/dt
      4368212 P/DT
L9          23 L6 AND P/DT

=> s l9 and py<=2002
      22503304 PY<=2002
L10         21 L9 AND PY<=2002

=> d l7 ibib abs hitstr tot

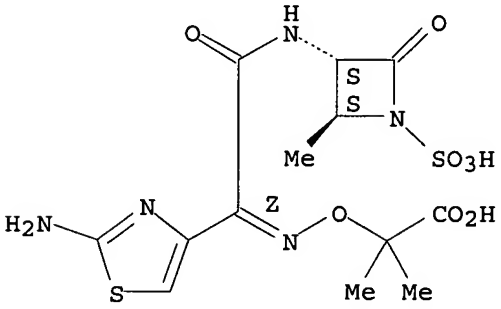
L7   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:120849  CAPLUS
DOCUMENT NUMBER:          140:163626
TITLE:                    Preparation of Aztreonam via hydrolysis of tert-butyl
                          Aztreonam with an aqueous acid
INVENTOR(S):              Gyollai, Viktor; Meszaros Sos, Erzsebet; Szabo, Csaba;
                          Singer, Claude; Salyi, Szabolcs
PATENT ASSIGNEE(S):       Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceutical
                          USA, Inc.
SOURCE:                   PCT Int. Appl., 17 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2004013133      A1   20040212       WO 2003-US24593  20030805
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
```

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004063682 A1 20040401 US 2003-635659 20030805
PRIORITY APPLN. INFO.: US 2002-400699P P 20020805
US 2002-401749P P 20020808
OTHER SOURCE(S): CASREACT 140:163626
AB The invention relates to a process for the synthesis of Aztreonam. Specifically, the process entails hydrolyzing [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-tert-butoxycarbonyl-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic acid (t-Bu Aztreonam) with an aqueous **mineral acid** to form Aztreonam.
IT **78110-38-0P**, Aztreonam
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of Aztreonam via hydrolysis of tert-Bu Aztreonam with an aqueous acid)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



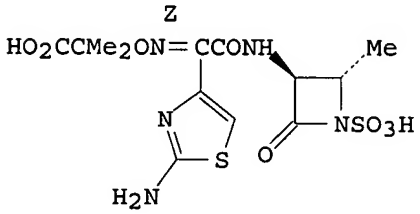
L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:410852 CAPLUS
DOCUMENT NUMBER: 99:10852
TITLE: Crystalline anhydrous form of [3S-(3α(Z),4β)]-3-([([2-amino-4-thiazolyl](1-carboxy-1-methylethoxy)imino)-acetyl]amino)-4-methyl-2-oxo-1-azetidinesulfonic acid and pharmaceutical composition containing it
INVENTOR(S): Floyd, David M.; Kocy, Octavian R.; Monkhouse, Donald C.; Pipkin, James D.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 70024	A1	19830119	EP 1982-106227	19820712
EP 70024	B1	19850626		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1181075	A1	19850115	CA 1982-405257	19820616
AU 8285010	A1	19830120	AU 1982-85010	19820618
AU 557096	B2	19861204		
ZA 8204418	A	19830427	ZA 1982-4418	19820622
JP 58023689	A2	19830212	JP 1982-118330	19820706
JP 03043273	B4	19910701		
IL 66286	A1	19860331	IL 1982-66286	19820709
AT 14016	E	19850715	AT 1982-106227	19820712
US 4946838	A	19900807	US 1986-888640	19860728

PRIORITY APPLN. INFO.: US 1981-282636 19810713
EP 1982-106227 19820712

GI



I

AB A crystalline anhydrous form (β) of the title compound (I) [78110-38-0] which is nonhygroscopic and has a greater stability than the hydrated crystalline form (α) is prepared by dissolving the α-form in an anhydrous organic solvent such as an alkanol or by treating the α form with an amine to form a salt and then precipitation of the β-form with a **mineral acid** or by conversion of the α-form to a silyl derivative and precipitation of the β-form by dilution with EtOH to hydrolyze the silyl derivative

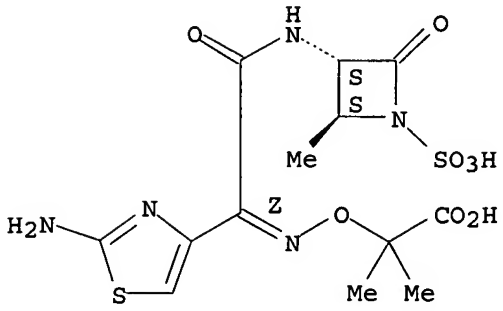
The α-I was recrystd. from 1:1 MeOH-H2O, washed with CH2Cl2 and Me2CO and redissolved in MeOH to give β-I. The α-I was also treated with AcN(SiMe3)2 [10416-58-7] and then EtOH to give β-I or α-I in EtOH was treated with Et3N [121-44-8] and then EtOH-HCl to give β-I. The β-I can be used for pharmaceutical formulation especially with addition of a basic material such as an amino acid.

IT **80581-95-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 80581-95-9 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

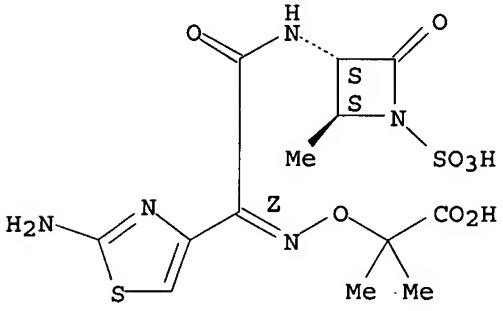
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

IT **78110-38-0P**
RL: THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, for pharmaceuticals)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> d l8 ibib abs hitstr tot

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:120849 CAPLUS
DOCUMENT NUMBER: 140:163626
TITLE: Preparation of Aztreonam via hydrolysis of tert-butyl Aztreonam with an **aqueous acid**
INVENTOR(S): Gyollai, Viktor; Meszaros Sos, Erzsebet; Szabó, Csaba; Singer, Claude; Salyi, Szabolcs
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceutical USA, Inc.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013133	A1	20040212	WO 2003-US24593	20030805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004063682	A1	20040401	US 2003-635659	20030805

PRIORITY APPLN. INFO.: US 2002-400699P P 20020805
US 2002-401749P P 20020808

OTHER SOURCE(S): CASREACT 140:163626

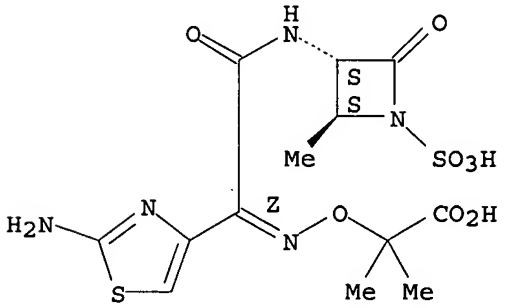
AB The invention relates to a process for the synthesis of Aztreonam. Specifically, the process entails hydrolyzing [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-tert-butoxycarbonyl-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic acid (t-Bu Aztreonam) with an aqueous mineral acid to form Aztreonam.

IT **78110-38-0P**, Aztreonam
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of Aztreonam via hydrolysis of tert-Bu Aztreonam with an **aqueous acid**)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> d l10 ibib abs hitstr tot

L10 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:935443 CAPLUS
DOCUMENT NUMBER: 136:58849
TITLE: Compositions and methods to improve the oral

absorption of antimicrobial agents
INVENTOR(S): Choi, Seung-Ho; Lee, Jeoung-Soo; Keith, Dennis
PATENT ASSIGNEE(S): Cubist Pharmaceuticals, Inc., USA; International Health Management Associates, Inc.; University of Utah Research Foundation
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097851	A2	20011227	WO 2001-US19625	20010618 <--
WO 2001097851	A3	20020516		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248360	B1	20010619	US 2000-598089	20000621 <--
EP 1294361	A2	20030326	EP 2001-944619	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012393	A	20030708	BR 2001-12393	20010618
JP 2003535911	T2	20031202	JP 2002-503335	20010618
US 2003039956	A1	20030227	US 2001-888114	20010622

PRIORITY APPLN. INFO.:

US 2000-598089	A	20000621
US 2001-829405	A	20010409
US 2001-283976P	P	20010416
WO 2001-US19625	W	20010618

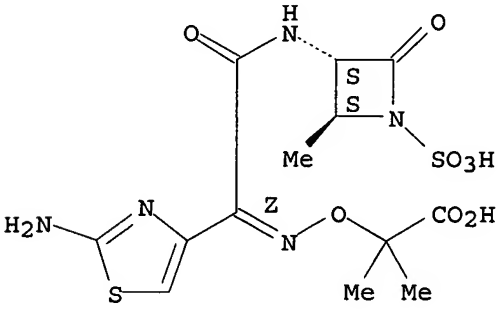
AB The present invention provides compns. and methods for increasing absorption of antibacterial agents, particularly third generation cephalosporin antibacterial agents, in oral dosage solid and/or suspension forms. Specifically, the composition is comprised of a biopolymer that is preferably swellable and/or mucoadhesive, an antimicrobial agent, and a cationic binding agent contained within the biopolymer such that the binding agent is ionically bound or complexed to at least one member selected from the group consisting of the biopolymer and the antimicrobial agent. A solution of 44.5 mg calcium chloride in 10 mL water and 1.0 g of ceftriaxone in 10 mL water was added gradually to a solution of 400 mg carrageenan and the dispersion was centrifuged and the supernatant was lyophilized. The resulting composition comprized carrageenan 27.7, ceftriaxone 1, and calcium chloride 3.1%. Plasma concentration of different antimicrobial-biopolymer complexes after oral administration to rats was measured.

IT **78110-38-0DP**, Aztreonam, conjugates with biopolymers and cationic binding agents
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. and methods to improve oral absorption of antimicrobial agents)

RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-

oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:564833 CAPLUS
DOCUMENT NUMBER: 135:152367
TITLE: Nitrate salts of antimicrobial agents
INVENTOR(S): Del Soldato, Piero; Benedini, Francesca; Antognazza, Patrizia
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2001054691	A1	20010802	WO 2001-EP430	20010116	<--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
IT 1317735	B1	20030715	IT 2000-MI92	20000126	
BR 2001007824	A	20021105	BR 2001-7824	20010116	<--
EP 1253924	A1	20021106	EP 2001-909631	20010116	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003520814	T2	20030708	JP 2001-554675	20010116	
US 2003105066	A1	20030605	US 2002-181424	20020724	

PRIORITY APPLN. INFO.: IT 2000-MI92 A 20000126
WO 2001-EP430 W 20010116
OTHER SOURCE(S): MARPAT 135:152367

AB Nitrate salts of antiviral, antifungal, and antibacterial agents such as acyclovir, tetracycline, etc. were prepared Growth inhibition of, e.g., an S. Aureus strain by title compds. was demonstrated.

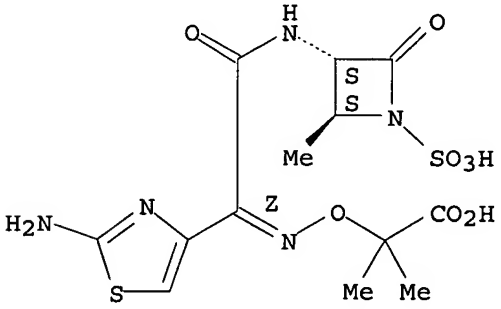
IT **352466-01-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitrate salts of antimicrobial agents)
RN 352466-01-4 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, nitrate (9CI) (CA INDEX NAME)

CM 1

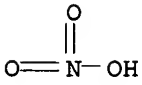
CRN 78110-38-0
CMF C13 H17 N5 O8 S2

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 7697-37-2
CMF H N O3



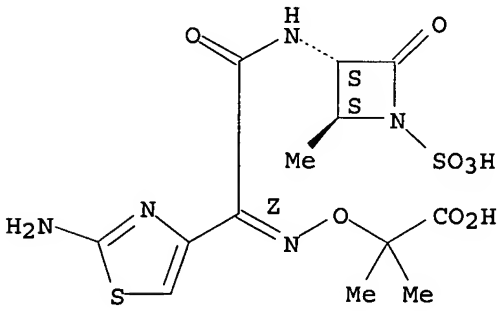
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:249881 CAPLUS
DOCUMENT NUMBER: 134:252200
TITLE: Preparation and isolation of azthreonam
INVENTOR(S): Oszczapowicz, Irena; Gumiezna, Teresa; Oszczapowicz, Janusz; Sikora, Adam; Szczesna, Iwona
PATENT ASSIGNEE(S): Instytut Biotechnologii i Antybiotykow, Pol.
SOURCE: Pol., 11 pp.
CODEN: POXXA7
DOCUMENT TYPE: **Patent**
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 178521	B1	20000531	PL 1995-311090	19951024 <--

PRIORITY APPLN. INFO.: PL 1995-311090 19951024
OTHER SOURCE(S): MARPAT 134:252200
AB The title compound was prepared by hydrolysis of azthreonam ester (alkyl, aralkyl or aryl ester; preferably tert-Bu ester) with carboxylic **acid** solution (such as CF3CO2H, CCl3CO2H and HCO2H) followed by isolation of high purity azthreonam from **acid** solution by addition of organic solvent and activated carbon, and removal of pure azthreonam from the activated carbon by rinsing with water.
IT **78110-38-0P**, Azthreonam
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and isolation of azthreonam)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

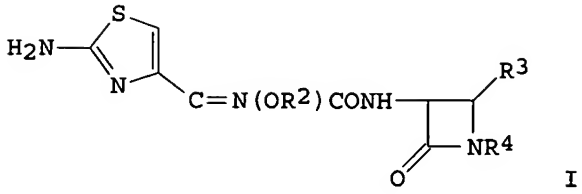
Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:580599 CAPLUS
DOCUMENT NUMBER: 119:180599
TITLE: Method for producing semisynthetic β-lactam antibiotics
INVENTOR(S): Borowicz, Piotr; Zukowski, Edward; Gorecki, Piotr; Cieplinska, Joanna; Szulc, Zofia
PATENT ASSIGNEE(S): Osrodek Badawczo-Rozwojowy Biotechnologii, Pol.
SOURCE: Pol., 20 pp.
CODEN: POXXA7
DOCUMENT TYPE: **Patent**
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 154681	B1	19910930	PL 1987-267518	19870831 <--

PRIORITY APPLN. INFO.: PL 1987-267518 19870831
OTHER SOURCE(S): MARPAT 119:180599
GI



I

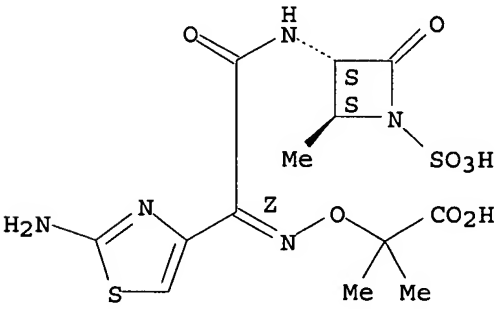
AB Title compds. having Z-configuration of alkoxyimino moiety I (R2 = H, alkyl, C≤5 cycloalkyl carboxyalkyl; R3 = H, C3 alkyl, β-(H2NCO2Me); R4 = H, HO, HO3S, HO3SO, HOP(O)OMe, HO(Me)P(O)O, MeNO2SNHCO protonated or as alkali metal salt, Me3Si, (substituted) 5-tetrazolyl, etc.; R3R4 = a group which with the β-lactam ring completes a Δ3-cephem-3-carboxylic **acid**), antibiotics (no data), are prepared 2-(2-Aminothiazol-4-yl)-2-(Z)-methoxyiminoacetic **acid** was reacted with PhCH2COBr to give the phenylacetamido derivative which was treated with SOCl2 to give the acetyl chloride derivative, which in turn was reacted with 7-amino-3-(acetoxymethylceph-3-en-4-carboxylic **acid** to give the cephem derivative which was enzymically hydrolyzed to remove the protective amino group and treated with anhydrous NaOAc to give (Z)-I (R2 = Me, R3R4 = group to complete Δ3-cephem-4-carboxylic **acid**).Na salt. Addnl. I were prepared

IT **149496-40-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibiotic)

RN 149496-40-2 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, [2α,3β(Z)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

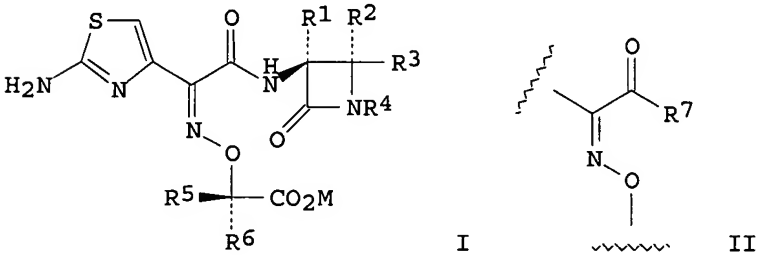


L10 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:214230 CAPLUS
DOCUMENT NUMBER: 116:214230
TITLE: Process and intermediates for beta-lactams having aminothiazole (iminooxyacetic **acid**)acetic **acid** sidechains
INVENTOR(S): Denzel, Theodor; Cimarusti, Christopher M.; Singh, Janak; Mueller, Richard H.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

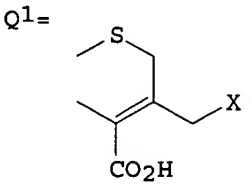
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 464705	A1	19920108	EP 1991-110748	19910628	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5194604	A	19930316	US 1990-546622	19900629	<--
CA 2043817	AA	19911230	CA 1991-2043817	19910604	<--
AU 9178163	A1	19920102	AU 1991-78163	19910605	<--
AU 645810	B2	19940127			
ZA 9104348	A	19920325	ZA 1991-4348	19910606	<--
IN 176439	A	19960525	IN 1991-DE510	19910611	<--
FI 9103138	A	19911230	FI 1991-3138	19910627	<--
NO 9102560	A	19911230	NO 1991-2560	19910628	<--
HU 58090	A2	19920128	HU 1991-2202	19910628	<--
HU 211083	B	19951030			
JP 04261175	A2	19920917	JP 1991-158322	19910628	<--
RU 2021270	C1	19941015	RU 1991-4895787	19910628	<--
PL 165404	B1	19941230	PL 1991-290856	19910628	<--
CN 1058593	A	19920212	CN 1991-105309	19910629	<--
CN 1029965	B	19951011			

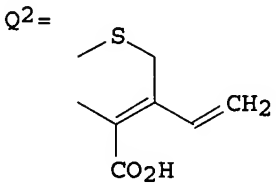
PRIORITY APPLN. INFO.: US 1990-546622 A 19900629
OTHER SOURCE(S): MARPAT 116:214230
GI



I

II





AB Title compds. [I; R1 = H, alkoxy; R2 = H, alkyl; R3 = H, alkyl, CH2O2CNH2; R4 = H, CH2(CO2H)C6H4OH-4, SO3M, OSO3M; R3R4 = Q1, Q2; R5, R6 = H, alkyl; R5R6C = cycloalkyl; M = H, cation; X = OH, OAc, Br, Cl, pyridinio], were prepared by condensation of the appropriate aminoazetidinone with **acid** derivative II (R7 = N-bound 4-7 membered heterocyclyl, heterocyclyloxy). Thus, (2S-trans)-3-amino-2-methyl-4-oxo-1-

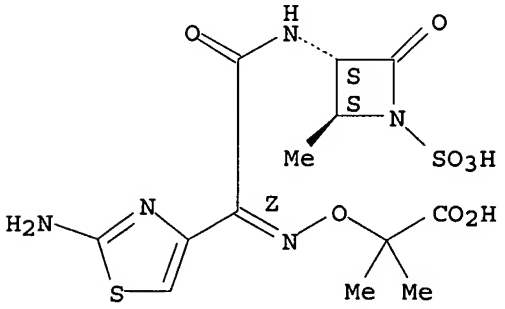
azetidinesulfonic **acid** inner salt (preparation given) in MeOH/H2O/Et3N at pH 8.0 and 0° was treated with (Z)-2-amino-α-[(1-carboxy-1-methylethoxy)imino]-4-thiazoleacetic **acid** 2,5-dioxo-1-pyrrolidinyl ester, methanesulfonate salt to give, after acidification to pH 4.3, [2S-[2α,3β(Z)]]-3-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-methyl-4-oxo-1-azetidinesulfonic **acid.**

IT **78110-38-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

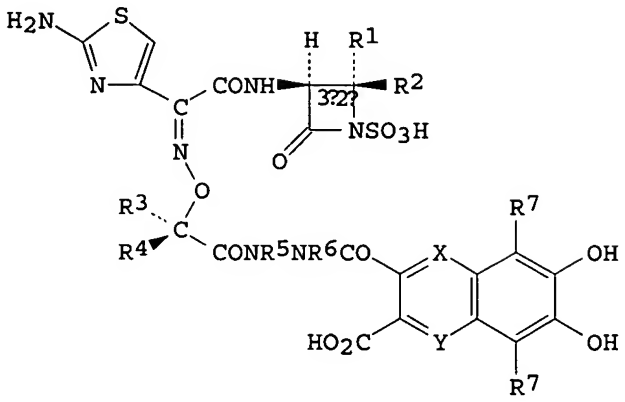
Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:440326 CAPLUS
DOCUMENT NUMBER: 113:40326
TITLE: Heteroaroylhydrazide derivatives of monocyclic β-lactam antibiotics
INVENTOR(S): Sundeen, Joseph Edward; Ermann, Peter Hans
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 342423	A2	19891123	EP 1989-107843	19890429 <--
EP 342423	A3	19910417		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4904775	A	19900227	US 1988-194355	19880516 <--
ZA 8903483	A	19900131	ZA 1989-3483	19890510 <--
DK 8902348	A	19891117	DK 1989-2348	19890512 <--
AU 8934847	A1	19891116	AU 1989-34847	19890516 <--
AU 618598	B2	19920102		
JP 02017189	A2	19900122	JP 1989-122705	19890516 <--
US 5037983	A	19910806	US 1989-444237	19891201 <--
AU 9185768	A1	19911205	AU 1991-85768	19911011 <--
AU 640531	B2	19930826		

PRIORITY APPLN. INFO.: US 1988-194355 19880516
OTHER SOURCE(S): MARPAT 113:40326
GI



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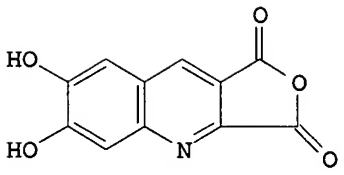

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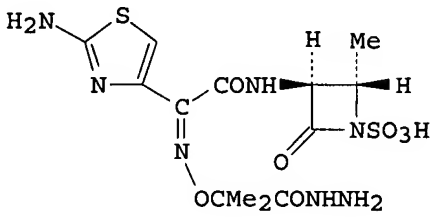


III

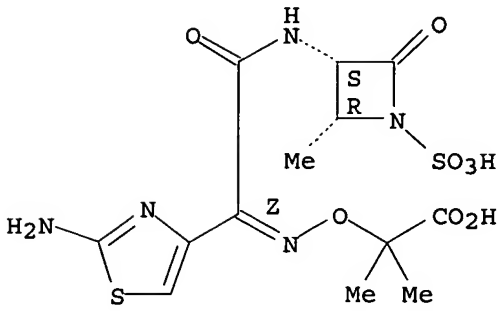
AB The title compds. (I; R1, R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R3, R4 = H, alkyl, R3R4 = alkylene; R5, R6 = H, alkyl; or R5R6 = C2-5 alkylene; R7 = H, F, Cl, Br; X, Y = N, CH), useful as bactericides against gram-pos. and gram-neg. organisms, are prepared A solution of 485 mg anhydride II in DMF was treated with a solution of 1.42 g hydrazide III (preparation given) in DMF at 25° and enough Et3N to raise pH to 7.5 to give 3.05 mg (2S,2'α,3'β)-(Z)-I (R1 = R3 = R4 = Me, R2 = R5 = R6 = R7 = H, X = N, Y = CH), and 135 mg isomer I (X = CH, Y = N). Also prepared were 7 addnl. I. I are effective in combating bacterial infection in mammals at 14-100 mg/kg-day.

IT **80951-91-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of bactericides)

RN 80951-91-3 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

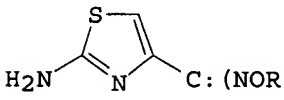


L10 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:178477 CAPLUS
Correction of: 1988:112060
DOCUMENT NUMBER: 112:178477
Correction of: 108:112060
TITLE: Copper-mediated oximation reaction for preparation of β-lactam antibiotics
INVENTOR(S): Sedegran, Thomas C.; Anderson, Carl F.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

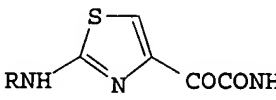
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 212392	A1	19870304	EP 1986-110654	19860801 <--
EP 212392	B1	19900627		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4675398	A	19870623	US 1985-766224	19850816 <--
CA 1268759	A1	19900508	CA 1986-514285	19860721 <--
AT 54147	E	19900715	AT 1986-110654	19860801 <--
JP 62042984	A2	19870224	JP 1986-190403	19860813 <--
JP 07068243	B4	19950726		

PRIORITY APPLN. INFO.: US 1985-766224 19850816
EP 1986-110654 19860801

GI



Q



I

AB β-Lactam-containing antibiotics which have an acylamino substituent Q (R1 = carboxyalkyl) are prepared wherein the ratio of syn/anti isomer is maximized by reacting I (R = amino protecting group, A = β-lactam nucleus) with H2NOR1 or a salt or ester thereof in presence of a Cu salt. To a solution of H2NOCHMe2CO2H and CuSO4.5H2O in H2O at pH 2.0 was added K (3S-trans)-3-[[[2-(formylamino)-4-thiazolyl]oxoacetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonate. The mixture was stirred 3 h at 30°,

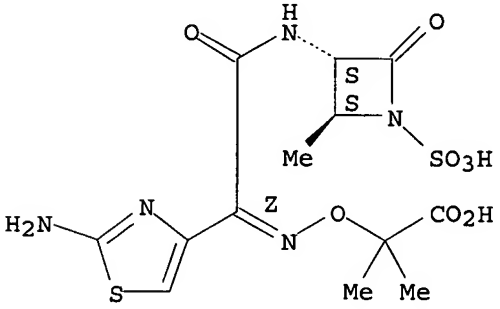
(CO2H)2 was added, the pH adjusted to 0.5, and the deformylation completed to give [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid.**

IT **78110-38-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via copper-mediated oximation)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:594450 CAPLUS
DOCUMENT NUMBER: 111:194450
TITLE: Preparation of 3-(acylamino)-1-sulfoazetidinones and their salts as antibacterial agents
INVENTOR(S): Sykes, Richard B.; Parker, William L.; Cimarusti, Christopher M.; Koster, William H.; Slusarchyk, William A.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: U.S., 70 pp. Cont.-in-part of U.S. Ser. No. 188,893, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4775670	A	19881004	US 1981-226562	19810119 <--
BE 887428	A1	19810806	BE 1981-203736	19810206 <--
DK 8100523	A	19810808	DK 1981-523	19810206 <--
DK 166280	B	19930329		
DK 166280	C	19930830		
FI 8100352	A	19810808	FI 1981-352	19810206 <--
FI 80271	B	19900131		
FI 80271	C	19900510		
SE 8100861	A	19810808	SE 1981-861	19810206 <--
SE 457954	B	19890213		
SE 457954	C	19890713		
NO 8100410	A	19810810	NO 1981-410	19810206 <--

NO 161065	B	19890320			
NO 161065	C	19890628			
AU 8166985	A1	19810813	AU 1981-66985	19810206	<--
AU 548896	B2	19860109			
GB 2071650	A	19810923	GB 1981-3655	19810206	<--
GB 2071650	B2	19841205			
DE 3104145	A1	19811217	DE 1981-3104145	19810206	<--
DE 3104145	C2	19990512			
ZA 8100808	A	19820224	ZA 1981-808	19810206	<--
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PL 126840	B1	19830930	PL 1981-229569	19810206	<--
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AT 8100550	A	19841215	AT 1981-550	19810206	<--
AT 378367	B	19850725			
RO 86528	B3	19850315	RO 1981-111297	19810206	<--
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IL 62082	A1	19860831	IL 1981-62082	19810206	<--
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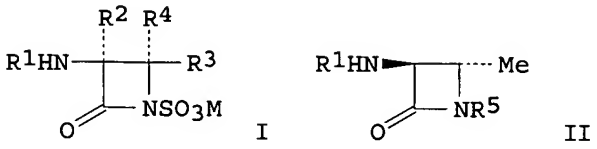
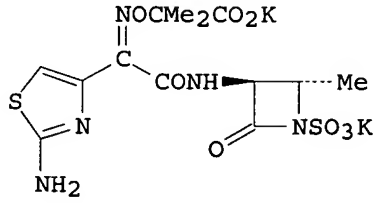
CA 1340253	A1	19981215	CA 1996-617057	19960828	<--

PRIORITY APPLN. INFO.:

US 1980-119276	A2	19800207
US 1980-188893	A2	19800929
US 1981-226562	A	19810119
US 1981-230837	A	19810202
AT 1981-550	A	19810206
CA 1981-370320	A3	19810206
CH 1981-816	A	19810206

CS 1981-909 A3 19810206
GB 1981-3655 A3 19810206
IN 1981-DE67 A1 19810206
OTHER SOURCE(S): CASREACT 111:194450; MARPAT 111:194450
GI





III

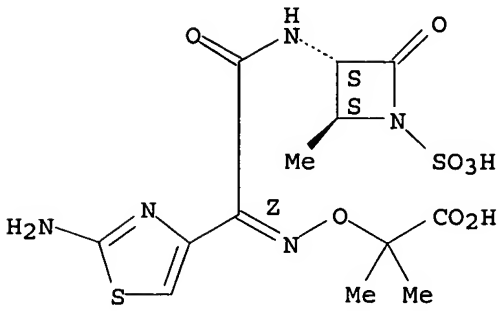
AB The title compds. [I; M = H, cation; R1 = H, carboxylic **acid** -derived acyl; R2 = H, alkoxy; R3, R4 = H, alkyl, cycloalkyl, (un)substituted Ph, or 1 of R3, R4 = H and the other = alkoxycarbonyl, 1-alkenyl, 1-alkynyl, CH:CHPh, C.tplbond.CPh] were prepared HOCHMeCH(NHCO2CMe3)CONHOCH2Ph (preparation given) was stirred .apprx.16 h in THF under N with Ph3P and EtO2CN:NCO2Et to give azetidinone II (R1 = Me3O2C, R5 = OCH2Ph) which was converted in 3 steps to II (R1 = PhCH2O2C, R5 = H). The latter was stirred 1 h with SO3 in DMF to give, after salt formation, II (R1 = PhCH2O2C, R5 = SO3- N+Bu4) which was hydrogenolyzed over Pd/C and the product stirred .apprx.16 h with (Z)-2-amino-α-[[1-[(diphenylmethoxy)carbonyl]-1-methylethoxy]imino]-4-thiazoleacetic **acid** in DMF containing DCC and N-hydroxybenzotriazole to give, after saponification, title compound III which had min. inhibitory concentration of <0.05 μg/mL against, e.g., Klebsiella pneumoniae 9527 and Proteus mirabilis 3855.

IT **78110-38-0P 80581-85-7P 80581-95-9P 80629-12-5P 123287-13-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibacterial agent)

RN 78110-38-0 CAPLUS

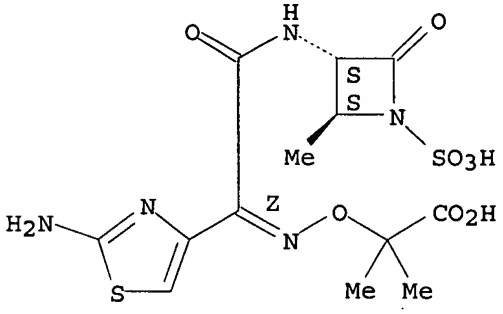
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 80581-85-7 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt (9CI) (CA INDEX NAME)

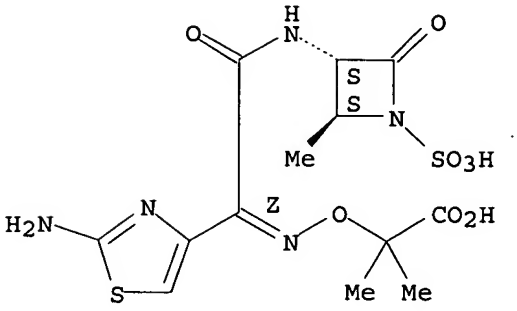
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 80581-95-9 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

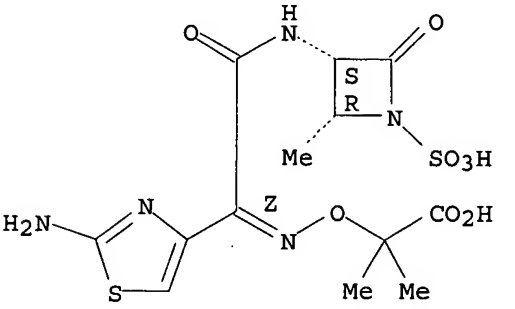
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

RN 80629-12-5 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

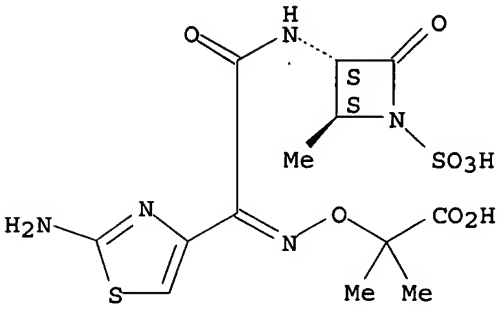
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

RN 123287-13-8 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, disodium salt, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



●2 Na

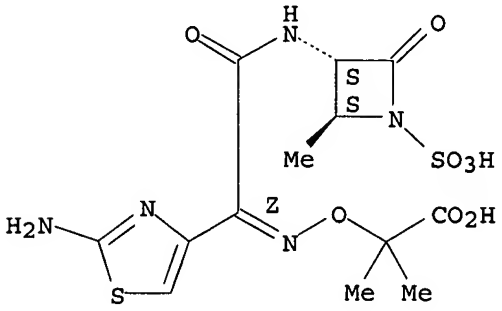
L10 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:514969 CAPLUS
DOCUMENT NUMBER: 111:114969
TITLE: Process for the enantioselective preparation of monobactam antibiotics from D-glyceraldehyde derivatives
INVENTOR(S): Herranz Herranz, Rosario; Hernandez Resa, Piedad; Nieves Elvira, Rosa Maria
PATENT ASSIGNEE(S): Antibioticos S. A., Spain
SOURCE: Span., 21 pp.
CODEN: SPXXAD
DOCUMENT TYPE: **Patent**
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2001459	A6	19880516	ES 1986-3439	19861215 <--

PRIORITY APPLN. INFO.: ES 1986-3439 19861215
OTHER SOURCE(S): MARPAT 111:114969
GI For diagram(s), see printed CA Issue.
AB Monobactams I [R1 = H, acyl; R2 = (un)substituted Me; M = H, cation] are prepared in 11 steps from D-glyceraldehyde derivs. D-R3OCH2CH(OR4)CHO (R3, R4 = OH-protecting groups). (R)-2,3-O-Isopropylideneglyceraldehyde was converted to the homologous α-amino nitrile, which underwent N-benzyloxycarbonylation, H2O2-assisted hydrolysis to the amide, O-deprotection, reprotection of 4-OH as the chloracetate, activation of 3-OH as the mesylate, and sulfonation-cyclization-deprotection to give (3S, 4R)-3-(benzyloxycarbonylamino)-4-hydroxymethyl-2-oxo-1-azetidinesulfonic **acid** as the Bu4N+ salt. This underwent O-phenoxycarbonylation, ammonolysis to the 4-CH2OCONH2 compound, hydrogenolytic N-deprotection of amino, and DCC/1-hydroxybenzotriazole-mediated amidation to give the di-Na salt of (3S, 4R)-3-[2-(2-amino-4-thiazolyl)-(Z)-2-(1-carboxy-1-methylethoxyimino)acetamido]-4-(carbamoyloxymethyl)-2-oxo-1-azetidinesulfonic **acid.**
IT **80581-86-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibiotic, from glyceraldehyde derivative)

RN 80581-86-8 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

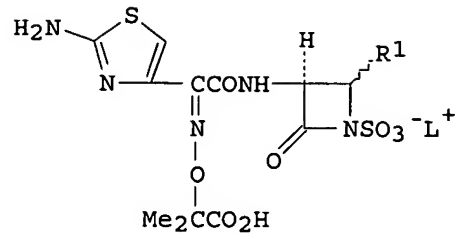


●2 Na

L10 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:131412 CAPLUS
DOCUMENT NUMBER: 108:131412
TITLE: Process for the preparation of (3S)-3[[(2-amino-4-thiazolyl)-[(1-carboxy-1-methyloxy)imino]acetyl]amino]-2-oxo-1-azetidinesulfonic **acids** as antibiotics
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Israeli, 24 pp.
CODEN: ISXXAQ
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 68919	A1	19870130	IL 1983-68919	19830608 <--

PRIORITY APPLN. INFO.: IL 1983-68919 19830608
GI



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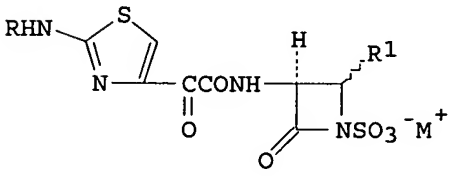


II

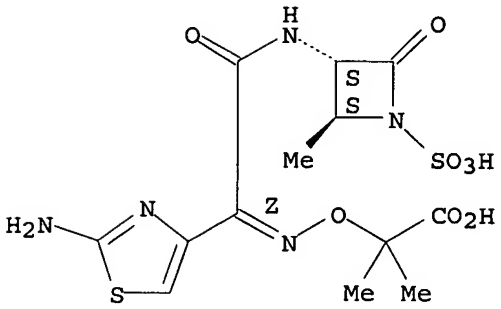
AB The title compds. I (R1 = H, C1-4 alkyl; L+ = H+, inorg. cation, substituted ammonium ion), useful as antibiotics (no data), are prepared by reacting azetidinone derivative II (R = H, amino-protecting group; R1 = as given above; M+ = inorg. cation, substituted ammonium ion) with Me2C(ONH2)CO2H (III) or a salt thereof. Formylation of 2-amino-4-thiazolylacetic **acid** in HCO2H and Ac2O gave 2-formylamino-4-thiazolylacetic **acid** which was condensed with (3S-trans)-3-amino-4-methyl-2-oxo-1-azetidinesulfonic **acid** to give, after workup, the corresponding thiazolylacetylaminoazetidinone derivative as a K salt. Oxid. of this azetidinone derivative (5.8 g) with Mn(OAc)2.4H2O in AcOH containing Ac2O gave 3.55 g (3S-trans)-3-[[2-(formylamino)-4-thiazolyl]-oxoacetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid** K salt. A mixture of (3S-trans)-3-[[2-amino-4-thiazolyl)oxoacetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid** K salt and III in H2O was kept at room temperature for 48 h to give , after workup, [3S-[3α(Z),4β]]-I (L+ = H+, R1 = Me).

IT **78110-38-0P 80581-85-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibiotic)

RN 78110-38-0 CAPLUS

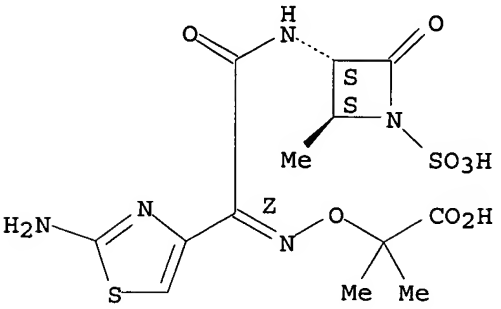
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 80581-85-7 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

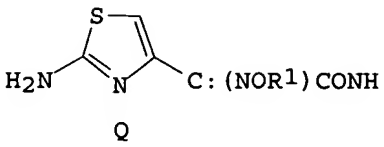


● Na

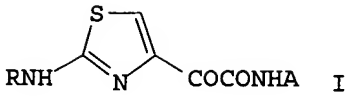
L10 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:112060 CAPLUS
DOCUMENT NUMBER: 108:112060
TITLE: Copper-mediated oximation reaction for preparation of β-lactam antibiotics
INVENTOR(S): Sedegran, Thomas C.; Anderson, Carl F.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 212392 A1		**19870304**	EP 1986-11065419860801	
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1985-766224	19850816

GI



Q



I

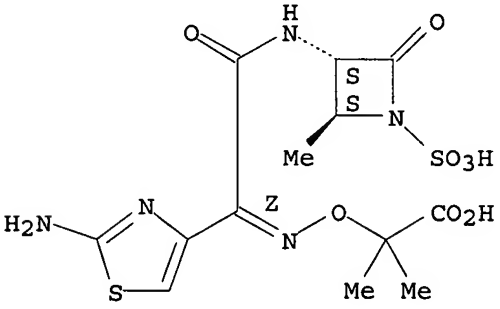
AB β-Lactam-containing antibiotics which have an acylamino substituent Q (R1 = carboxyalkyl) are prepared wherein the ratio of syn-/anti isomer is maximized by reacting I (R = amino protecting group, A = β-lactam nucleus) with H2NOR1 or a salt or ester thereof in presence of a Cu salt. To a solution of H2NOCHMe2CO2H and CuSO4.5H2O in H2O at pH 2.0 was added K (3S-trans)-3-[[[2-(formylamino)-4-thiazolyl]oxoacetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonate. The mixture was stirred 3 h at 30°, (CO2H)2 was added, the pH adjusted to 0.5, and the deformylation completed to give [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid.**

IT **78110-38-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via copper-mediated oximation)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

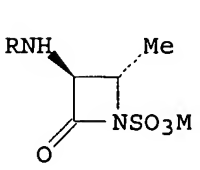


L10 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:37491 CAPLUS
DOCUMENT NUMBER: 108:37491
TITLE: Process for the preparation of [3,4-(trans)]-3-acylamino-4-methyl-2-oxo-1-azetidinesulfonic **acid** derivatives and their pharmaceutically acceptable salts
INVENTOR(S): Perez-Aranda Ortega, Agustin; Herranz Herranz, Rosario; Arribas Mocoroa, Enrique; Fernandez Resa, Piedad; Conde Ruzafa, Santiago; Nieves Elvira, Rosa; Roncal Serra, Fernando; Fernandez Sousa-Faro, Jose Maria
PATENT ASSIGNEE(S): Antibioticos S. A., Spain
SOURCE: Span., 40 pp.
CODEN: SPXXAD

DOCUMENT TYPE: **Patent**
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 549891	A1	19860401	ES 1985-549891	19851212 <--

PRIORITY APPLN. INFO.: ES 1985-549891 19851212
GI



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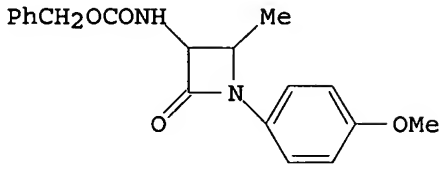
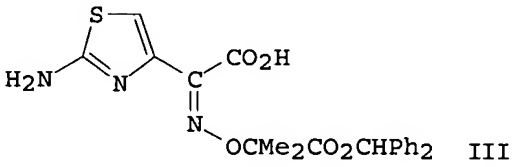
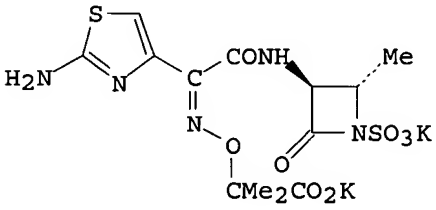


II



III



IV

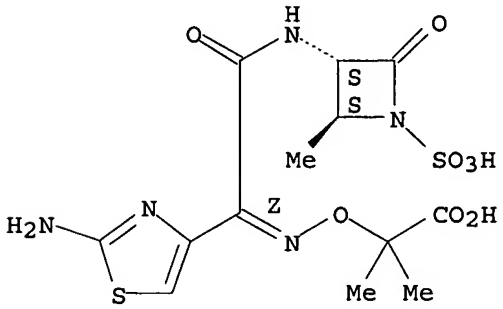
AB The antibiotic title compds. (I; R = H, acyl; M= H, alkali metal, quaternary ammonium) are prepared by a 9-step synthesis. For example, MeCOC(:NOH)CO2Et was reduced by Al amalgam and protected with PhCH2OCOCl to give MeCOCH(NHCO2CH2Ph)CO2Et, which was condensed with 4-H2NC6H4OMe and reduced with NaBH3CN/ZnCl2 to give 4-MeOC6H4NHCHMeCH(NHCO2CH2Ph)CO2Et. This was cyclized with PhMgBr (base) to give oxoazetidine derivative cis-II, which was epimerized by NaI/Me3SiCl/Et3N to give trans-II. The latter underwent N-deprotection with (NH4)2Ce(NO3)6, N-sulfonation with SO3-DMF complex in DMF, and hydrogenolysis over Pd/C to give I (R = M = H), which underwent amidation with thiazolylacetic **acid** derivative III in the presence of N-hydroxybenzotriazole and DCC, followed by deprotection with CF3CO2H/anisole and conversion, to give (thiazolylacetylamino)azetidinesulfonate salt IV (i.e., the racemic di-K salt of aztreonam).

IT **80581-95-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, from oximinoacetylacetate)

RN 80581-95-9 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

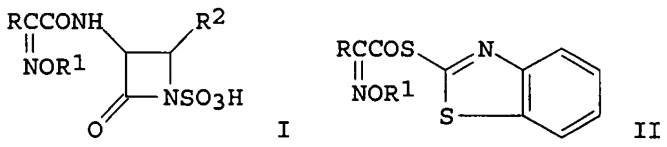


●2 K

L10 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:554164 CAPLUS
DOCUMENT NUMBER: 107:154164
TITLE: Preparation of antimicrobial 1-sulfo-2-oxoazetidinecarboxylic **acid** derivatives via catalytic ester cleavage and pharmaceuticals containing them
INVENTOR(S): Furlenmeier, Andre; Hofheinz, Werner; Hubschwerlen, Christian N.; Isenring, Hans P.
PATENT ASSIGNEE(S): Hoffmann-La Roche, Inc., USA
SOURCE: U.S., 32 pp. Division of U.S. Ser. No. 499,595.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4652651	A	19870324	US 1986-852046	19860414 <--
US 4948898	A	19900814	US 1989-317081	19890228 <--

PRIORITY APPLN. INFO.: US 1983-499595 19830531
US 1986-852046 19860414
US 1986-926742 19861103
OTHER SOURCE(S): CASREACT 107:154164
GI



I II

AB Title compds. I (R = amino-substituted 5- or 6-membered heteroaryl containing 1-2 N and an optional S or O; R1 = H, alkyl, phenylalkyl, alkanoyl, alkoxycarbonyl, etc.; R2 = H, alkyl, alkenyl, alkynyl, alkoxycarbonyl,

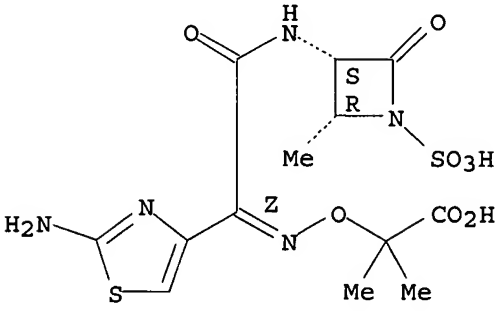
HON:CH, H2NCO, etc.) and their hydrolyzable esters and salts, useful as antimicrobials, were prepd by acylation of an aminoazetidinone with a thioester II. The preparation of II and the preparation of the carboxylic **acids** RC(CO2H):NOCH2CO2C(R3)3 (III; R3 = C1-3 alkyl) is given. (3S,4R)-4-Ethynyl-3-tritylamino-2-azetidinone was hydrogenated over Pd/C to the Et derivative which was sulfonated with a SO3-pyridinium complex to the azetidinesulfonic **acid** derivative, which was acylated with the appropriate thioester; catalytic cleavage of this ester gave Na (3S,4R)-3-[(Z)-2-(2-amino-4-thiazolyl)-2-(methoxyimino)acetamido]-4-ethyl-2-oxo-1-azetidinesulfonate (IV). The min. inhibitory concentration of IV against Proteus mirabilis or P. vulgaris was ≤0.05 μg/mL. An ampul for i.m. administration was prepared from a lyophilizate of a specific I.

IT **89707-65-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antimicrobial)

RN 89707-65-3 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● Na

L10 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:90168 CAPLUS
DOCUMENT NUMBER: 106:90168
TITLE: Sodium salts of β-lactam antibiotics
INVENTOR(S): Palomo Coll, Alberto; Cabre Castellvi, Juan
PATENT ASSIGNEE(S): Gema S. A., Spain
SOURCE: Span., 19 pp.
CODEN: SPXXAD
DOCUMENT TYPE: **Patent**
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 526971	A1	19860201	ES 1983-526971	19831102 <--

PRIORITY APPLN. INFO.: ES 1983-526971 19831102

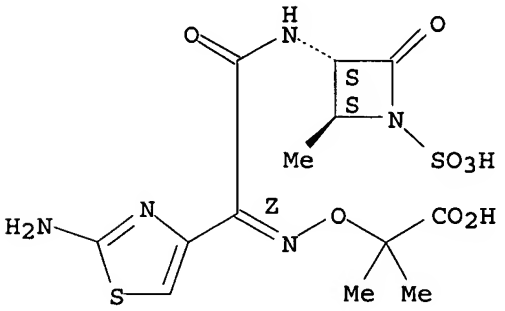
AB The title salts are prepared by treating the **acid** form of the antibiotic with alkyl acetoacetate Na salt or Na N-substituted acetoacetamide in iso-PrOH in the presence of an amine. Thus, 4.04 g ampicillin in a mixture of 10 mL CH2Cl2 and 5 mL iso-PrOH was treated at 0-5° with 2.2 mL Et3N, followed by the addition of 2.03 g iso-Pr acetoacetate Na salt, to give 97.3% ampicillin Na.

IT **80581-86-8P**
RL: PREP (Preparation)
(preparation of, by neutralization of azthreonam)

RN 80581-86-8 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 Na

L10 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:423220 CAPLUS
DOCUMENT NUMBER: 101:23220
TITLE: 1-Sulfo-2-oxoazetidines
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Jpn. Kokai Tokkyo Koho, 88 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

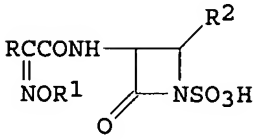
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 59021681	A2	19840203	JP 1983-98151	19830603	<--
JP 03016951	B4	19910306			
DK 8302418	A	19831204	DK 1983-2418	19830527	<--
ZA 8303882	A	19840829	ZA 1983-3882	19830527	<--
ZA 8303887	A	19841128	ZA 1983-3887	19830527	<--
AU 8315068	A1	19831215	AU 1983-15068	19830530	<--
AU 558593	B2	19870205			
IL 68817	A1	19890815	IL 1983-68817	19830530	<--
HU 29165	O	19840130	HU 1983-1952	19830601	<--
ES 522886	A1	19850416	ES 1983-522886	19830601	<--

HU 194844	B	19880328	HU 1985-4699	19830601 <--
NO 8302001	A	19831205	NO 1983-2001	19830602 <--
FI 8302004	A	19831204	FI 1983-2004	19830603 <--
ES 529772	A1	19850716	ES 1984-529772	19840216 <--
ES 529773	A1	19850801	ES 1984-529773	19840216 <--
ES 529775	A1	19850801	ES 1984-529775	19840216 <--
ES 529774	A1	19851101	ES 1984-529774	19840216 <--
US 4816582	A	19890328	US 1987-111480	19871022 <--

PRIORITY APPLN. INFO.:

CH 1982-3416	19820603
CH 1982-3417	19820603
CH 1983-2201	19830425
CH 1983-2320	19830429
US 1983-499971	19830601
US 1986-835395	19860303

GI



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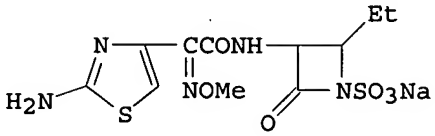


II

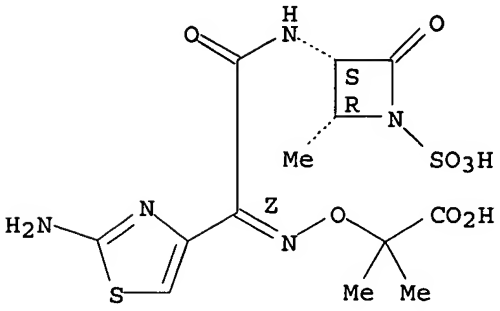
AB Title compds I (R = substituted heterocycle; R1 = H, alkyl, alkanoyl, alkoxycarbonyl; R2 = H, alkyl, alkenyl, alkynyl, alkoxycarbonyl, alkoxyiminomethyl, carbamoyl) and their salts were prepared Thus, stirring 18 mg (3S,4S)-3-amino-2-oxo-4-propyl-1-azatidinesulfonic **acid** with 32 mg 2-(2-amino-4-thiazolyl)-2(Z)-methoxyiminoacetic **acid** 2-benzthiazolylthio ester and 14.5 mg Et3N in CH2Cl2 gave 35 mg (3S,4S)-3-[(Z)-2-(2-amino-4-thiazolyl-2-(methoxyimino)acetamido]-2-oxo-4-propyl-1-azetidinesulfonate thiethylamine salt. (3S,4R)-II has a min inhibitory concentration of 0.1 μg/mL against K. pneumoniae 418.

IT **89707-65-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 89707-65-3 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

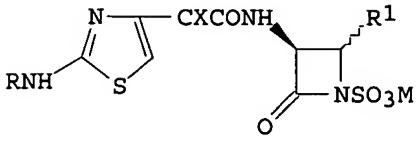


● Na

L10 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:174529 CAPLUS
DOCUMENT NUMBER: 100:174529
TITLE: Azetidinesulfonic **acids**
INVENTOR(S): Moniot, Jerome L.; Cimarusti, Christopher M.; Fox, Rita T.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 97352	A2	19840104	EP 1983-106005	19830620 <--
EP 97352	A3	19840912		
EP 97352	B1	19871007		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4704457	A	19871103	US 1982-390728	19820621 <--
CA 1205076	A1	19860527	CA 1983-427829	19830510 <--
AU 8314499	A1	19840105	AU 1983-14499	19830512 <--
AU 563938	B2	19870730		
ZA 8303623	A	19840229	ZA 1983-3623	19830519 <--
JP 59007190	A2	19840114	JP 1983-100110	19830603 <--
JP 03048910	B4	19910725		
DK 8302807	A	19831222	DK 1983-2807	19830617 <--
DK 163510	B	19920309		
DK 163510	C	19920727		
NO 8302229	A	19831222	NO 1983-2229	19830620 <--
HU 29994	O	19840228	HU 1983-2191	19830620 <--
HU 190903	B	19861228		
ES 523420	A1	19850316	ES 1983-523420	19830620 <--
AT 30155	E	19871015	AT 1983-106005	19830620 <--
HU 194558	B	19880229	HU 1983-1046	19830620 <--
HU 194560	B	19880229	HU 1986-1047	19830620 <--
ES 537960	A1	19851101	ES 1984-537960	19841126 <--
DK 9101465	A	19910814	DK 1991-1465	19910814 <--
DK 166322	B	19930405		
DK 166322	C	19930823		

DK 9201065 A 19920827 DK 1992-1065 19920827 <--
DK 166209 B 19930322
DK 166209 C 19930816
PRIORITY APPLN. INFO.: US 1982-390728 19820621
EP 1983-106005 19830620
OTHER SOURCE(S): CASREACT 100:174529
GI



I

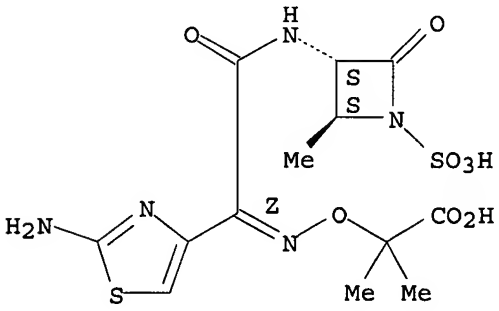
AB Azetidinesulfonates I (X = NOCMe2CO2H, R = H, R1 = H, alkyl, M = cation) were prepared from I (X = O). Thus, 2-amino-4-thiazoleacetic **acid** was N-formylated and used to acylate aminoazetidine to give I (R = CHO, R1 = α-Me, X = H2, M = K)(II). KMnO4 oxidation of II (X = H2) gave II (X = O) which was treated with H2NOCMe2CO2H and deformylated to give [3S-[3α(Z),4β]]-I (X = NOCMe2CO2H, R = H, R1 = Me, M = H).

IT **78110-38-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1984:174525 CAPLUS
DOCUMENT NUMBER: 100:174525
TITLE: 1-Sulfo-2-oxoazetidine derivatives
INVENTOR(S): Furlenmeier, Andre; Hubschwerlen, Christian Nicolas; Hofheinz, Werner; Isenring, Hans Peter
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 149 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3

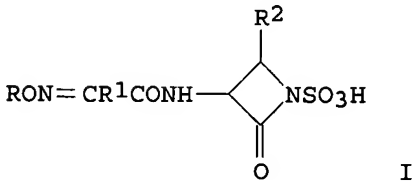
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 96297	A2	19831221	EP 1983-105155	19830525 <--
EP 96297	A3	19840411		
EP 96297	B1	19880615		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 35135	E	19880715	AT 1983-105155	19830525 <--
DK 8302418	A	19831204	DK 1983-2418	19830527 <--
ZA 8303882	A	19840829	ZA 1983-3882	19830527 <--
ZA 8303887	A	19841128	ZA 1983-3887	19830527 <--
AU 8315068	A1	19831215	AU 1983-15068	19830530 <--
AU 558593	B2	19870205		
IL 68817	A1	19890815	IL 1983-68817	19830530 <--
HU 29165	O	19840130	HU 1983-1952	19830601 <--
ES 522886	A1	19850416	ES 1983-522886	19830601 <--
HU 194844	B	19880328	HU 1985-4699	19830601 <--
NO 8302001	A	19831205	NO 1983-2001	19830602 <--
FI 8302004	A	19831204	FI 1983-2004	19830603 <--
ES 529772	A1	19850716	ES 1984-529772	19840216 <--
ES 529773	A1	19850801	ES 1984-529773	19840216 <--
ES 529775	A1	19850801	ES 1984-529775	19840216 <--
ES 529774	A1	19851101	ES 1984-529774	19840216 <--
US 4816582	A	19890328	US 1987-111480	19871022 <--

PRIORITY APPLN. INFO.:

CH 1982-3416	19820603
CH 1982-3417	19820603
CH 1983-2201	19830425
CH 1983-2320	19830429
EP 1983-105155	19830525
US 1983-499971	19830601
US 1986-835395	19860303

GI



I

AB Bactericidal azetidinesulfonic **acids** I [R = H, alkanoyl, alkoxycarbonyl, alkenyl, (un)substituted alkyl; R1 = heteroaryl; R2 = H, alkynyl, R3ON:CH2, (un)substituted alkyl, alkenyl; R3 = H, alkyl] were prepared Thus, S-2-benzothiazolyl (Z)-2-amino-α-(methoxyimino)-4-thiazoleethanethioate was treated with (2R,3S)-3-amino-2-ethyl-4-oxo-1-azetidinesulfonic **acid** [prepared in 4 steps from 4-(methylsulfonyl)-3-(tritylamino)-2-azetidinone] to give (Z)-(2R,3S)-I Na salt (R = Me, R1 = 2-amino-4-thiazolyl, R2 = Et) (II). Against, e.g., Proteus mirabilis 2117 II had a min. inhibitory concentration of ≤0.05 μg/mL.

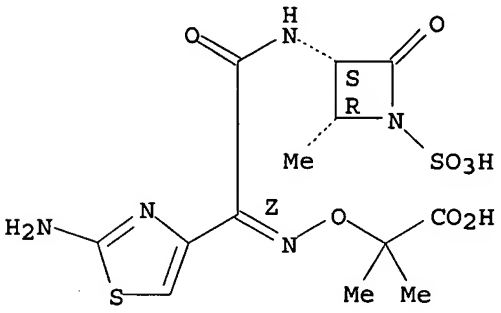
IT **89707-65-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 89707-65-3 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-

azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● Na

L10 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:6197 CAPLUS
DOCUMENT NUMBER: 100:6197
TITLE: (3S)-3-[(2-Amino-4-thiazolyl)[[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-oxo-1-azetidinesulfonic **acid** and 4-substituted derivatives
INVENTOR(S): Cimarusti, Christopher M.; Fox, Rita T.; Fritz, Alan W.; Koster, William H.; Moniot, Jerome L.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 86556	A1	19830824	EP 1983-300191	19830114 <--
EP 86556	B1	19860507		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4443374	A	19840417	US 1982-344895	19820201 <--
AT 19631	E	19860515	AT 1983-300191	19830114 <--
CA 1196335	A1	19851105	CA 1983-420362	19830127 <--
JP 58134090	A2	19830810	JP 1983-13621	19830129 <--
JP 03012065	B4	19910219		

PRIORITY APPLN. INFO.: US 1982-344895 19820201
EP 1983-300191 19830114
OTHER SOURCE(S): CASREACT 100:6197
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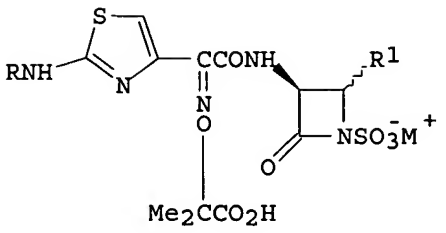


I

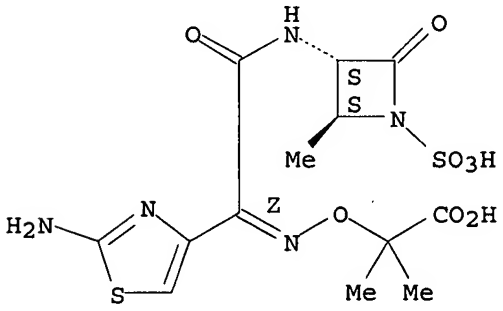
AB Title lactams I (R = H, protecting group; R1 = H, Me, Et; M = H, cation) were prepared as bactericides (no data). Thus, treating 2-amino-4-thiazolylglyoxylic **acid** Et3N salt with Ph2P(O)Cl gave a mixed anhydride which was treated with 3S-trans-3-amino-4-methyl-2-oxo-1-azetidinesulfonic **acid** and then with H2NOCHMeCO2H to give I (R = H, R1 = 2-Me, M = K).

IT **78110-38-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 78110-38-0 CAPLUS

CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



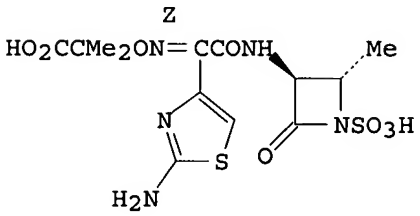
L10 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1983:410852 CAPLUS
DOCUMENT NUMBER: 99:10852
TITLE: Crystalline anhydrous form of [3S-(3α(Z),4β)]-3-([([2-amino-4-thiazolyl](1-carboxy-1-methylethoxy)imino)-acetyl]amino)-4-methyl-2-oxo-1-azetidinesulfonic **acid** and pharmaceutical composition containing it
INVENTOR(S): Floyd, David M.; Kocy, Octavian R.; Monkhouse, Donald C.; Pipkin, James D.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 70024	A1	19830119	EP 1982-106227	19820712 <--
EP 70024	B1	19850626		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1181075	A1	19850115	CA 1982-405257	19820616 <--
AU 8285010	A1	19830120	AU 1982-85010	19820618 <--
AU 557096	B2	19861204		
ZA 8204418	A	19830427	ZA 1982-4418	19820622 <--
JP 58023689	A2	19830212	JP 1982-118330	19820706 <--
JP 03043273	B4	19910701		
IL 66286	A1	19860331	IL 1982-66286	19820709 <--
AT 14016	E	19850715	AT 1982-106227	19820712 <--
US 4946838	A	19900807	US 1986-888640	19860728 <--

PRIORITY APPLN. INFO.: US 1981-282636 19810713
EP 1982-106227 19820712

GI



I

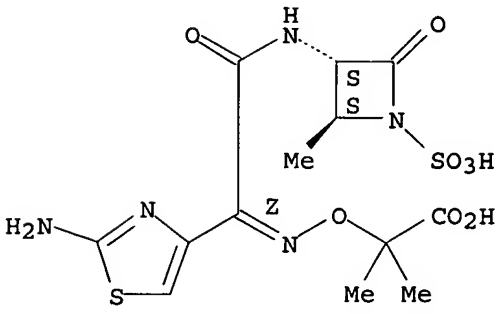
AB A crystalline anhydrous form (β) of the title compound (I) [78110-38-0] which is nonhygroscopic and has a greater stability than the hydrated crystalline form (α) is prepared by dissolving the α-form in an anhydrous organic solvent such as an alkanol or by treating the α form with an amine to form a salt and then precipitation of the β-form with a mineral **acid** or by conversion of the α-form to a silyl derivative and precipitation of the β-form by dilution with EtOH to hydrolyze the silyl derivative
The α-I was recrystd. from 1:1 MeOH-H2O, washed with CH2Cl2 and Me2CO and redissolved in MeOH to give β-I. The α-I was also treated with AcN(SiMe3)2 [10416-58-7] and then EtOH to give β-I or α-I in EtOH was treated with Et3N [121-44-8] and then EtOH-HCl to give β-I. The β-I can be used for pharmaceutical formulation especially with addition of a basic material such as an amino **acid.**

IT **80581-95-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 80581-95-9 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

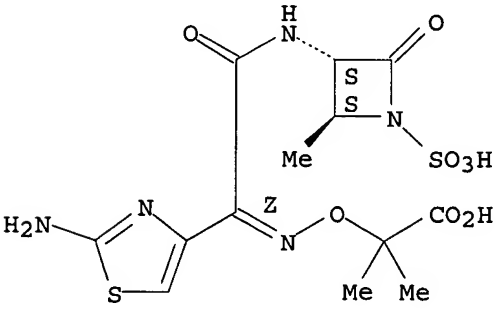
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

IT **78110-38-0P**
RL: THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, for pharmaceuticals)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:492116 CAPLUS
DOCUMENT NUMBER: 97:92116
TITLE: β-Lactam antibiotics
INVENTOR(S): Sykes, Richard Brook; Parker, William Lawrence; Cimarusti, Christopher Michael; Koster, William Henry; Slusarchyk, William Allen; Fritz, Alan William; Floyd, David Mack
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 139 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

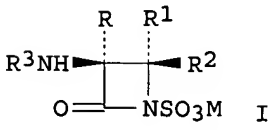
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 48953	A2	19820407	EP 1981-107572	19810923 <--
EP 48953	A3	19820818		
EP 48953	B1	19880309		
R: IT				
US 4775670	A	19881004	US 1981-226562	19810119 <--
CH 653993	A	19860131	CH 1981-5565	19810206 <--
EP 187355	A1	19860716	EP 1985-116364	19810923 <--
R: IT				
US 4386034	A	19830531	US 1982-347595	19820210 <--
GB 2139618	A1	19841114	GB 1983-33191	19831213 <--
GB 2139618	B2	19850501		
AT 8402169	A	19851015	AT 1984-2169	19840705 <--
AT 380472	B	19860526		
AT 8402168	A	19860115	AT 1984-2168	19840705 <--
AT 381089	B	19860825		
US 4625022	A	19861125	US 1985-798356	19851115 <--

PRIORITY APPLN. INFO.:

US 1980-188893	A	19800929
US 1981-226562	A	19810119
US 1981-230837	A	19810202
US 1980-119276	A2	19800207
AT 1981-550	A	19810206
CH 1981-816	A	19810206
GB 1981-3655	A3	19810206
EP 1981-107572	P	19810923

OTHER SOURCE(S): CASREACT 97:92116

GI



I

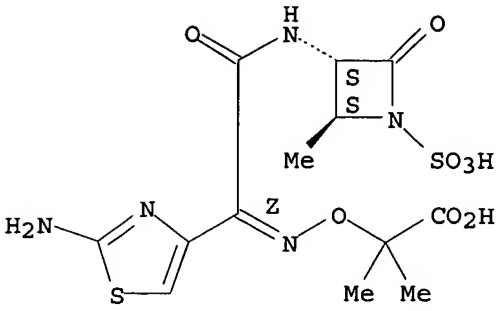
AB Lactams I [R = H, alkoxy; R1, R2 = H, (un)substituted alkyl, cycloalkyl, Ph, alkoxycarbonyl; R3 = acyl; M = H, cation] were prepared Thus tert-butoxycarbonylallothreonine was treated with PhCH2ONH2 and cyclized to the azetidinone which was deblocked and treated with ClCO2CH2Ph to give (±)-cis-3-benzyloxycarbonylamino-2-azetidinone (II). Sulfonylation of II, followed by deblocking and acylation with PhCH2CO2H, gave I (R = R1 = H, R2 = Me, R3 = PhCH2CO, M = K) which had min inhibitory concentration against Staphylococcus aureus of 25 μg/mL.

IT **80581-95-9P 80629-12-5P 82691-17-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and bactericidal activity of)

RN 80581-95-9 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

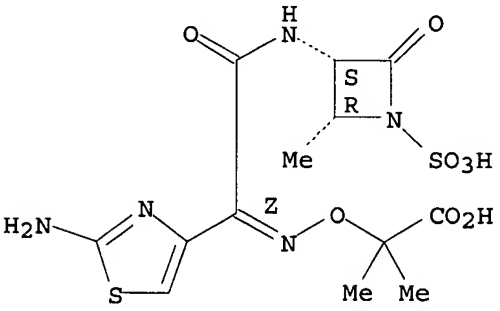
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

RN 80629-12-5 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

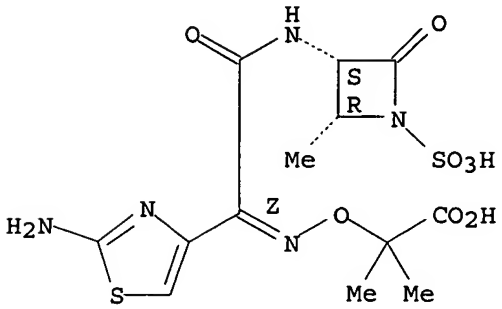
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

RN 82691-17-6 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2α,3α(Z)]- (9CI) (CA INDEX NAME)

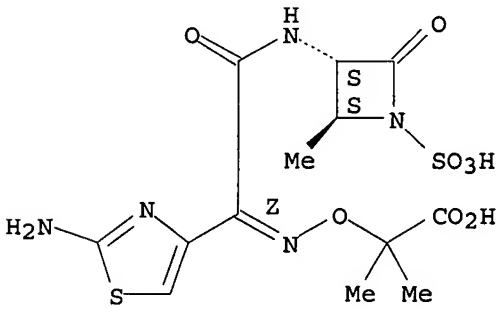
Relative stereochemistry.
Double bond geometry as shown.



●2 K

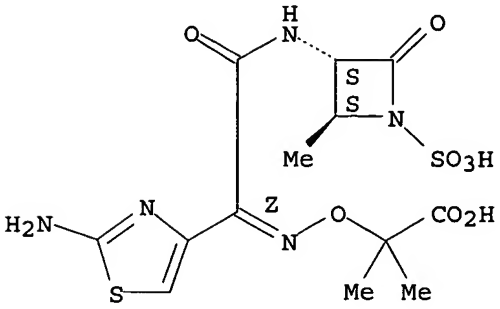
IT **78110-38-0P 80581-85-7P 80581-86-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 80581-85-7 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt (9CI) (CA INDEX NAME)

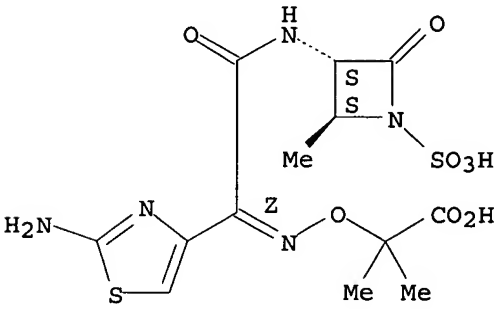
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 80581-86-8 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 Na

L10 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:181062 CAPLUS
DOCUMENT NUMBER: 96:181062
TITLE: Antibiotic β-lactams
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Neth. Appl., 117 pp.
CODEN: NAXXAN
DOCUMENT TYPE: **Patent**
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 8100571	A	19810901	NL 1981-571	19810206 <--
NL 192924	B	19980105		

NL 192924	C	19980507			
BE 887428	A1	19810806	BE 1981-203736	19810206	<--
DK 8100523	A	19810808	DK 1981-523	19810206	<--
DK 166280	B	19930329			
DK 166280	C	19930830			
FI 8100352	A	19810808	FI 1981-352	19810206	<--
FI 80271	B	19900131			
FI 80271	C	19900510			
SE 8100861	A	19810808	SE 1981-861	19810206	<--
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NO 8100410	A	19810810	NO 1981-410	19810206	<--
NO 161065	B	19890320			
NO 161065	C	19890628			
AU 8166985	A1	19810813	AU 1981-66985	19810206	<--
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ES 499171	A1	19820601	ES 1981-499171	19810206	<--
DD 156180	C	19820804	DD 1981-227473	19810206	<--
FR 2509299	A1	19830114	FR 1981-2372	19810206	<--
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AT 8100550	A	19841215	AT 1981-550	19810206	<--
AT 378367	B	19850725			
RO 86528	B3	19850315	RO 1981-111297	19810206	<--
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HU 191029	B	19861228			
CH 651020	A	19850830	CH 1981-816	19810206	<--
CH 653993	A	19860131	CH 1981-5565	19810206	<--
CS 244105	B2	19860717	CS 1981-909	19810206	<--
IL 62082	A1	19860831	IL 1981-62082	19810206	<--
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CS 244146	B2	19860717	CS 1984-9615	19841211	<--
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JP 06070006	B4	19940907			
CA 1340253	A1	19981215	CA 1996-617057	19960828	<--

PRIORITY APPLN. INFO.:

US 1980-119276	A	19800207
US 1980-188893	A	19800929
AT 1981-550	A	19810206
CA 1981-370320	A3	19810206
CH 1981-816	A	19810206
CS 1981-909	A3	19810206
GB 1981-3655	A3	19810206
IN 1981-DE67	A1	19810206

OTHER SOURCE(S): CASREACT 96:181062

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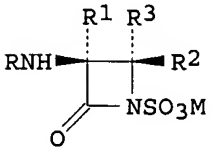

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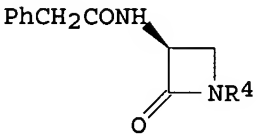


II

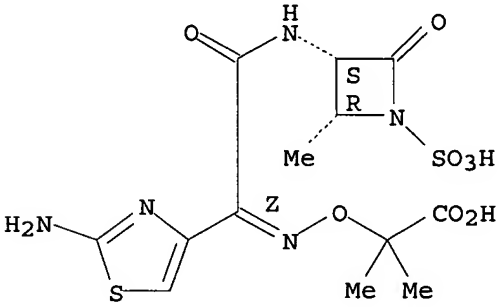
AB β-Lactams I (R = H, acyl; R1 = H, alkoxy; R2, R3 = H, alkyl, cycloalkyl, Ph, alkenyl, styryl, alkynyl, alkoxy, alkylthio, alkoxycarbamyl, CO2H, CH2OH, alkylsulfonylmethyl, arylsulfonylmethyl, halomethyl, CH2SH, CH2SCH2Ph, CH2SCPh3, CH2N3, CH2NH2; M = H, cation) were prepared Thus Na penicillin G was dethiolated with Raney Ni to give II [R4 = CH(CO2H)CHMe2] which was oxidized to II [R4 = CH(OAc)CHMe2]. NaBH4 reduction of the latter compound gave II (R4 = H) which was treated with pyridine-SO3 and KOH to give II (R4 = SO3K). II (R4 = SO3K) had a min. of inhibitory concentration against Staphylococcus aureus 1276 of 1.6 μg/mL.

IT **80629-12-5P 82691-17-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and bactericidal activity of)

RN 80629-12-5 CAPLUS

CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2R-[2α,3α(Z)]]- (9CI) (CA INDEX NAME)

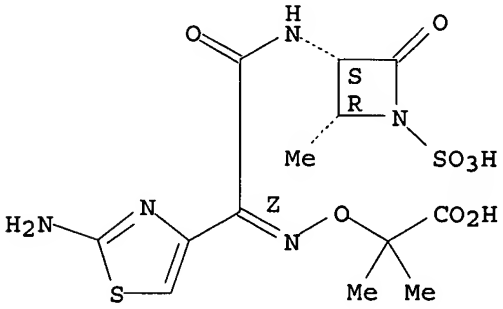
Absolute stereochemistry.
Double bond geometry as shown.



●2 K

RN 82691-17-6 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2α,3α(Z)]- (9CI) (CA INDEX NAME)

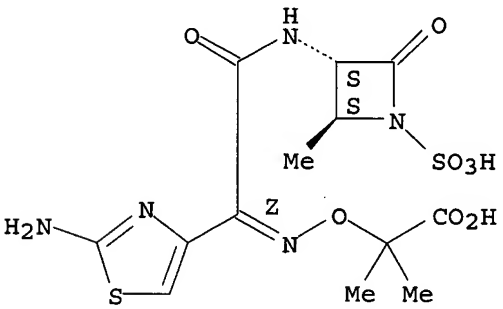
Relative stereochemistry.
Double bond geometry as shown.



●2 K

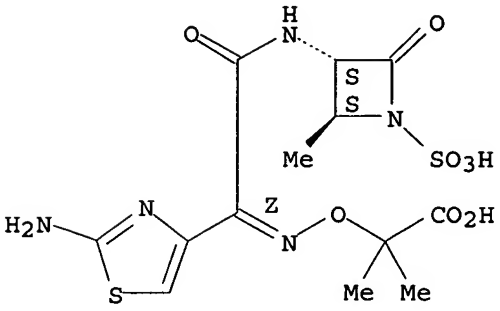
IT **78110-38-0P 80581-85-7P 80581-86-8P**
80581-95-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 78110-38-0 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 80581-85-7 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, monosodium salt (9CI) (CA INDEX NAME)

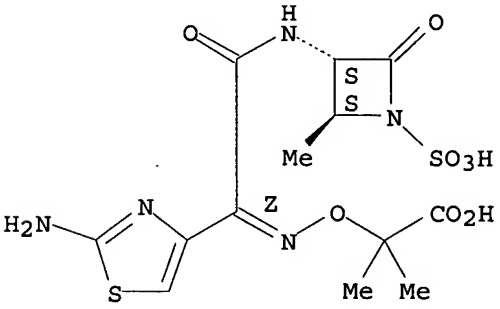
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 80581-86-8 CAPLUS
CN Propanoic acid, 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, disodium salt (9CI) (CA INDEX NAME)

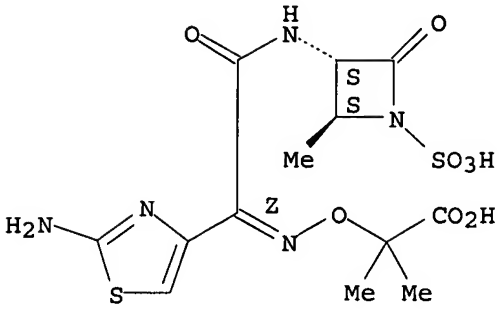
Absolute stereochemistry.
Double bond geometry as shown.



●2 Na

RN 80581-95-9 CAPLUS
CN Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, dipotassium salt, [2S-[2α,3β(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 K

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=> d l13 ibib abs hitstr tot

L13  ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN

10635659
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ACCESSION NUMBER: 2004:120849 CAPLUS
DOCUMENT NUMBER: 140:163626
TITLE: Preparation of **Aztreonam** via hydrolysis of tert-butyl **Aztreonam** with an aqueous **acid**
INVENTOR(S): Gyollai, Viktor; Meszaros Sos, Erzsebet; Szabo, Csaba; Singer, Claude; Salyi, Szabolcs
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceutical USA, Inc.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013133	A1	20040212	WO 2003-US24593	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063682	A1	20040401	US 2003-635659	20030805

PRIORITY APPLN. INFO.: US 2002-400699P P 20020805
US 2002-401749P P 20020808
OTHER SOURCE(S): CASREACT 140:163626
AB The invention relates to a **process** for the synthesis of **Aztreonam.** Specifically, the **process** entails hydrolyzing [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-tert-butoxycarbonyl-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid** (t-Bu **Aztreonam**) with an aqueous mineral **acid** to form **Aztreonam.**

L13 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:719333 CAPLUS
DOCUMENT NUMBER: 139:250284
TITLE: Coupling low-molecular substances to a modified polysaccharide, especially lactonized and/or oxidized hydroxyethyl starch for the preparation of drug formulation
INVENTOR(S): Orlando, Michele; Hemberger, Juergen
PATENT ASSIGNEE(S): Biotechnologie - Gesellschaft Mittelhessen MbH, Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003074088 A2 20030912 WO 2003-EP2084 20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10209822 A1 20030925 DE 2002-10209822 20020306
PRIORITY APPLN. INFO.: DE 2002-10209822 A 20020306

AB The invention relates to a method for coupling low-mol. substances to a starch-derived modified polysaccharide. The binding interaction between the modified polysaccharide and the low-mol. substance is based on a covalent bond which is the result of a coupling reaction between the terminal aldehyde group or a functional group of the modified polysaccharide mol. resulting from the chemical reaction of this aldehyde group and a functional group of the low-mol. substance which reacts with this aldehyde group or with the resulting functional group of the polysaccharide mol. The bond directly resulting from the coupling reaction can be optionally modified by a further reaction to the aforementioned covalent bond. The invention further relates to pharmaceutical compns. that comprise conjugates formed in this coupling **process** and to the use of said conjugates and compns. for the prophylaxis or therapy of the human or animal body.

L13 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:500974 CAPLUS
DOCUMENT NUMBER: 140:107427
TITLE: Effect of D240G substitution in a novel ESBL CTX-M-27
AUTHOR(S): Bonnet, R.; Recule, C.; Baraduc, R.; Chanal, C.; Sirot, D.; De Champs, C.; Sirot, J.
CORPORATE SOURCE: Laboratoire de Bacteriologie, Service de Bacteriologie-Virologie, Faculte de Medecine, Clermont-Ferrand, 63001, Fr.
SOURCE: Journal of Antimicrobial Chemotherapy (2003), 52(1), 29-35
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Escherichia coli clin. strain Gre-1 collected in 2000 from a French hospital harbored a novel CTX-M-encoding gene, designated blaCTX-M-27. CTX-M-27 differed from CTX-M-14 only by the substitution D240G and was the third CTX-M enzyme harboring this mutation after CTX-M-15 and CTX-M-16. The Gly-240-harboring enzyme CTX-M-27 conferred to E. coli higher MICs of ceftazidime (MIC, 8 vs. 1 mg/L) than did the Asp-240-harboring CTX-M-14 enzyme. Comparison of CTX-M-14 and CTX-M-27 showed that residue Gly-240 decreased Km for ceftazidime (205 vs. 940 μM), but decreased hydrolytic activity against good substrates, such as cefotaxime (kcat, 113 vs. 415 s-1), probably owing to the alteration of β3 strand positioning during the catalytic **process.**

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173602 CAPLUS

DOCUMENT NUMBER: 138:187560
TITLE: Method for producing crystalline anhydrous β-form of **Aztreonam**
INVENTOR(S): Chandiran, Thakashina Moorthy; Yennam, Satyanarayana; Ramesh, Dandala; Meenakshi, Sunderam Sivakumaraa
PATENT ASSIGNEE(S): Aurobindo Pharma Ltd., India
SOURCE: PCT Int. Appl., 6 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018578	A1	20030306	WO 2002-IN169	20020821

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

PRIORITY APPLN. INFO.: IN 2001-MA700 A 20010827

AB A **process** is described for producing anhydrous β-form of 2-[[(Z)-[1-(2-amino-4-thiazolyl)-2-[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]amino]-2-oxoethylidene]amino]oxy]-2-methylpropanoic **acid**, a.k.a. **Aztreonam**. Thus, the α-form of **Aztreonam**, which typically contains 7-14% water, was added to pre-cooled absolute EtOH at 8-10° and stirred for 30 min. to obtain a clear solution The solution was treated with activated carbon for 15 min at 8-10° and the suspension was then filtered through celite and washed with EtOH. The filtrate was warmed to 50-55° over a 2 h period to crystallize the β-form, then the hot suspension was cooled to 15-20°, stirred for 1 h, filtered and dried in vacuo to obtain the desired anhydrous β-form of **Aztreonam**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:750331 CAPLUS
DOCUMENT NUMBER: 139:62535
TITLE: Rate-Limited Steps of Human Oral Absorption and QSAR Studies
AUTHOR(S): Zhao, Yuan H.; Abraham, Michael H.; Le, Joelle; Hersey, Anne; Luscombe, Chris N.; Beck, Gordon; Sherborne, Brad; Cooper, Ian
CORPORATE SOURCE: Department of Chemistry, University College London, London, WC1H 0AJ, UK
SOURCE: Pharmaceutical Research (2002), 19(10), 1446-1457
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose. To classify the dissoln. and diffusion rate-limited drugs and establish quant. relationships between absorption and mol. descriptors. Methods. Absorption consists of kinetic transit **processes** in which dissoln., diffusion, or perfusion **processes** can become the rate-limited step. The absorption data of 238 drugs have been classified into either dissoln. or diffusion rate-limited based on an equilibrium method developed from solubility, dose, and percentage of absorption. A nonlinear

absorption model derived from first-order kinetics has been developed to identify the relationship between percentage of drug absorption and mol. descriptors. Results. Regression anal. was performed between percentage of absorption and mol. descriptors. The descriptors used were ClogP, mol. polar surface area, the number of hydrogen-bonding acceptors and donors, and Abraham descriptors. Good relationships were found between absorption and Abraham descriptors or ClogP. Conclusions. The absorption models can predict the following three BCS (Biopharmaceutics Classification Scheme) classes of compds.: class I, high solubility and high permeability; class III, high solubility and low permeability; class IV, low solubility and low permeability.

The absorption models overpredict the absorption of class II, low solubility and high permeability compds. because dissoln. is the rate-limited step of absorption.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:310125 CAPLUS
DOCUMENT NUMBER: 136:337024
TITLE: Predicting evolutionary potential: In vitro evolution accurately reproduces natural evolution of the TEM β-lactamase
AUTHOR(S): Barlow, Miriam; Hall, Barry G.
CORPORATE SOURCE: Biology Department, University of Rochester, Rochester, NY, 14627-0211, USA
SOURCE: Genetics (2002), 160(3), 823-832
CODEN: GENTAE; ISSN: 0016-6731
PUBLISHER: Genetics Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the validity of the authors' in vitro evolution method as a model for natural evolutionary **processes**, the TEM-1 β-lactamase gene was evolved in vitro and was selected for increased resistance to cefotaxime, cefuroxime, ceftazadime, and **aztreonam**, i.e., the "extended-spectrum" phenotype. The amino **acid** substitutions recovered in 10 independent in vitro evolvants were compared with the amino **acid** substitutions in the naturally occurring extended-spectrum TEM alleles. Of the 9 substitutions that have arisen multiple times in naturally occurring extended-spectrum TEM alleles, 7 were recovered multiple times in vitro. The authors take this result as evidence that their in vitro evolution technique accurately mimics natural evolution and can therefore be used to predict the results of natural evolutionary **processes**. Addnl., the results predict that a phenotype not yet observed among TEM β-lactamases in nature, resistance to cefepime, is likely to arise in nature.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:545723 CAPLUS
DOCUMENT NUMBER: 135:142230
TITLE: High purity lipopeptides, lipopeptide micelles and **processes** for preparing same
INVENTOR(S): Kelleher, Thomas J.; Lai, Jan-ji; Decourcey, Joseph P.; Lynch, Paul D.; Zenoni, Maurizio; Tagliani, Auro R.
PATENT ASSIGNEE(S): Cubist Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053330	A2	20010726	WO 2001-US1748	20010118
WO 2001053330	A3	20020418		
WO 2001053330	C2	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6696412	B1	20040224	US 2000-735191	20001128
BR 2001007731	A	20021001	BR 2001-7731	20010118
EP 1252179	A2	20021030	EP 2001-903121	20010118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003520807	T2	20030708	JP 2001-553802	20010118
NO 2002003476	A	20020920	NO 2002-3476	20020719

PRIORITY APPLN. INFO.:
US 2000-177170P P 20000120
US 2000-735191 A 20001128
WO 2001-US1748 W 20010118

AB The invention discloses highly purified daptomycin and to pharmaceutical compns. comprising this compound The invention discloses a method of purifying daptomycin comprising the sequential steps of anion exchange chromatog., hydrophobic interaction chromatog. and anion exchange chromatog. The invention also discloses a method of purifying daptomycin by modified buffer enhanced anion exchange chromatog. An improved method for producing daptomycin by fermentation of Streptomyces roseosporus is described. The invention also discloses HPLC methods for anal. of daptomycin purity. Methods of using lipopeptide micelles for purifying lipopeptide antibiotics, such as daptomycin, and using them therapeutically are disclosed. Thus, daptomycin was produced in a fermentation culture of S. roseosporus and partially purified daptomycin (9.9 Kg) was purified by microfiltration from 5500 L of fermentation broth. The partially purified daptomycin was further purified and resulted in a bulk daptomycin preparation with a purity of 91%. The daptomycin preparation contained 14 impurities as determined by HPLC anal. The daptomycin preparation was applied to a Poros P150 anion exchange resin (PE Biosystems) in Tris buffer pH 7.0 containing 6M urea and allowed to bind to the resin. The resin was washed with 3 column vols. of buffer prior to initiation of a NaCl gradient in the same buffer. Alternatively, the contaminants can be effectively removed from the column with a fixed salt level of 30 mM NaCl. The elution of purified daptomycin from the resin occurred at approx. 300 mM NaCl during a 0 to 1000 mM NaCl gradient. Daptomycin eluted from the column was greater than 99% pure as measured by the "first" HPLC method. The purified daptomycin contained only one detectable daptomycin contaminant. Anhydrodaptomycin and B-isomer were undetectable (<0.01% contamination). The level of the unidentified contaminant was 0.1-0.5%.

L13 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:527755 CAPLUS

DOCUMENT NUMBER: 135:266637
TITLE: Is There a Difference between Leads and Drugs? A Historical Perspective
AUTHOR(S): Oprea, Tudor I.; Davis, Andrew M.; Teague, Simon J.; Leeson, Paul D.
CORPORATE SOURCE: AstraZeneca R&D Molndal EST Lead Informatics, Moelndal, S 431 83, Swed.
SOURCE: Journal of Chemical Information and Computer Sciences (2001), 41(5), 1308-1315
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To be considered for further development, lead structures should display the following properties: (1) simple chemical features, amenable for chemical optimization; (2) membership to an established SAR series; (3) favorable patent situation; and (4) good absorption, distribution, metabolism, and excretion (ADME) properties. There are two distinct categories of leads: those that lack any therapeutic use (i.e., "pure" leads), and those that are marketed drugs themselves but have been altered to yield novel drugs. We have previously analyzed the design of leadlike combinatorial libraries starting from 18 lead and drug pairs of structures (S. J. Teague et al. Angew. Chemical, Int. Ed. Engl. 1999, 38, 3743-3748). Here, we report results based on an extended dataset of 96 lead-drug pairs, of which 62 are lead structures that are not marketed as drugs, and 75 are drugs that are not presumably used as leads. We examined the following properties: MW (mol. weight), CMR (the calculated mol. refractivity), RNG (the number of rings), RTB (the number of rotatable bonds), the number of hydrogen bond donors (HDO) and acceptors (HAC), the calculated logarithm of the n-octanol/water partition (CLogP), the calculated logarithm of the distribution coefficient at pH 7.4 (LogD74), the Daylight-fingerprint druglike score (DFPS), and the property and pharmacophore features score (PPFS). The following differences were observed between the medians of drugs and leads: ΔMW = 69; ΔCMR = 1.8; ΔRNG = ΔHAC =1; ΔRTB = 2; ΔCLogP = 0.43; ΔLogD74 = 0.97; ΔHDO = 0; ΔDFPS = 0.15; ΔPPFS = 0.12. Lead structures exhibit, on the average, less mol. complexity (less MW, less number of rings and rotatable bonds), are less hydrophobic (lower CLogP and LogD74), and less druglike (lower druglike scores). These findings indicate that the **process** of optimizing a lead into a drug results in more complex structures. This information should be used in the design of novel combinatorial libraries that are aimed at lead discovery.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:339085 CAPLUS
DOCUMENT NUMBER: 136:49150
TITLE: Evolution of TEM β-lactamase genes identified by PCR with newly designed primers in Korean clinical isolates
AUTHOR(S): Lee, S. H.; Jeong, S. H.; Lee, K. J.
CORPORATE SOURCE: Department of Genetic Engineering, Youngdong University, Chungbuk, 370-701, S. Korea
SOURCE: Clinical Microbiology and Infection (2001), 7(2), 98-100
CODEN: CMINFM; ISSN: 1198-743X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors isolated and sequenced β-lactamase (bla) genes from several different species of bacteria and used the sequences to analyze evolutionary changes among them. Nucleotide sequences of PCR primers for detecting 20 different alleles of the gene bla are provided. In the **process**, the authors discovered a new form of the bla gene, blaTEM-17b, which is distinct from blaTEM-17. The sequence of this new gene was submitted to GenBank. Sequence anal. suggests the in vivo evolution of β-lactamase genes (from blaTEM-1b to blaTEM-17b and from blaTEM-17b to blaTEM-52) under selective pressure of antimicrobial therapy.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:259972 CAPLUS
DOCUMENT NUMBER: 132:293042
TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): General Mills, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021504	A1	20000420	WO 1999-US20905	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2345815	AA	20000420	CA 1999-2345815	19991006
AU 9963872	A1	20000501	AU 1999-63872	19991006
EP 1119345	A1	20010801	EP 1999-951433	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527375	T2	20020827	JP 2000-575480	19991006

PRIORITY APPLN. INFO.:
US 1998-103700P P 19981009
US 1998-109696P P 19981124
US 1999-233443 A 19990120
WO 1999-US20905 W 19991006

AB A liquid encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liquid plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liquid plasticizer and the encapsulation of the active encapsulant is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous **process** to produce discrete, solid particles. The liquid content of the liquid encapsulant component provides substantially all or completely all of the liquid plasticizer needed to

plasticize the matrix component to obtain a formable, extrudable, cuttable, mixture or dough. Removal of liquid plasticizer prior to extrusion is not needed to adjust the viscosity of the mixture for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform its intended function. Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:417148 CAPLUS
DOCUMENT NUMBER: 129:172373
TITLE: Effect of an Amino **Acid** Insertion into the Omega Loop Region of a Class C β-Lactamase on Its Substrate Specificity
AUTHOR(S): Nukaga, Michiyoshi; Taniguchi, Kazuo; Washio, Yukio; Sawai, Tetsuo
CORPORATE SOURCE: Division of Microbial Chemistry Faculty of Pharmaceutical Sciences, Chiba University, Chiba, 263, Japan
SOURCE: Biochemistry (1998), 37(29), 10461-10468
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extended-substrate specificity of Enterobacter cloacae GC1 β-lactamase is entirely due to a three amino **acid** insertion after position 207. To clarify the reason for the extended-substrate specificity, Ala, Ala-Ala, Ala-Ala-Ala, and Ala-Ala-Ala-Ala were inserted after position 207 on the basis of the class C β-lactamase from E. cloacae P99, resp. The kcat and Km values of all the mutant enzymes for cephalothin, benzylpenicillin and ampicillin were almost the same as those of the wild-type enzyme, except for those of P99-210-4A which were decreased 4-15-fold. On the other hand, the kcat and Km values for oxyimino β-lactams such as cefuroxime, ceftazidime, and **aztreonam** increased with increasing nos. of inserted alanines. The kcat values of the mutant enzymes for cefuroxime increased 140-7400-fold compared with that of the wild-type. The Km values also increased with almost the same magnitude, resulting in about the same kcat/Km values as that of the wild-type. On progressive inhibition anal. of **aztreonam** of the mutant enzymes, two kinds of inactive acyl-enzyme with distinct stabilities were observed, and the proportion of the less stable inactive enzyme increased with increasing nos. of inserted alanines. This suggests that the extension of the substrate specificity is due to instability of the acyl-intermediate caused by an increased deacylation rate in the reaction **process.**

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:246882 CAPLUS
DOCUMENT NUMBER: 122:101409
TITLE: Surveillance of multidrug-resistant environmental bacteria
AUTHOR(S): Fukuchi, Kunihiko
CORPORATE SOURCE: Sch. Med., Showa Univ., Tokyo, 142, Japan

SOURCE: Rinsho Byori (1994), 42(11), 1111-18
CODEN: RBYOAI; ISSN: 0047-1860
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The multidrug-resistance of Staphylococcus epidermidis and Pseudomonas aeruginosa was surveyed. The multidrug-resistant S. epidermidis isolated accounted for 18% of the total S. epidermidis in 1991-1992 and were frequently isolated from specimens of the urine and respiratory system. The PCR revealed the existence of the mecA gene in S. epidermidis showing various degree of antibiotic resistance, suggesting that S. epidermidis is in the **process** of achieving multidrug resistance. The multidrug-resistant P. aeruginosa were isolated from 14.6% of the total P. aeruginosa in 1992-1993 and were most frequently isolated from the urine. Most of the multidrug resistant P. aeruginosa showed serotype E, suggesting the relationship between serotype and acquirement of drug resistance. Pulse-field electrophoresis of SpeI digested P. aeruginosa genomic DNA showed a characteristic pattern and the genome pattern should be applicable for the epidemiol.

L13 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:600516 CAPLUS
DOCUMENT NUMBER: 121:200516
TITLE: Characterization and amino **acid** sequence of IRT-4, a novel TEM-type enzyme with a decreased susceptibility to β-lactamase inhibitors
AUTHOR(S): Brun, Thierry; Peduzzi, Jean; Canica, Manuela Marin; Paul, Gerard; Nevot, Pierre; Barthelemy, Michel; Labia, Roger
CORPORATE SOURCE: CHU Cochin, Laboratoire de Bacteriologie, 75014, Paris, Fr.
SOURCE: FEMS Microbiology Letters (1994), 120(1-2), 111-18
CODEN: FMLED7; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The clin. isolate Escherichia coli PEY was highly resistant to amoxycillin, ticarcillin and piperacillin associated to β-lactamase inhibitors such as clavulanic **acid**, sulbactam, tazobactam and brobactam but susceptible to cephalosporins, **aztreonam** and imipenem. The susceptibility to mecillinam indicated that this phenotype was not related to hyperprodn. of the TEM-1 β-lactamase. E. coli PEY produced a new plasmid-mediated inhibitor-resistant β-lactamase of pI 5.2, which was named IRT-4. The determination of the amino **acid** sequence (Swiss-Prot accession number, P00810) of the purified protein indicated that IRT-4 differed from TEM-1 by two substitutions: Leu for Met-69 (ABL numbering) and Asp for Asn-276. A Met-69-Leu variant of TEM-1, obtained by site-directed mutagenesis, has been described as resistant to clavulanate. The Asp for Asn-276 substitution has not been reported previously. The side chains of Asp-276 and Arg-244 were expected to interact. Detns. of 50% inhibitory concns. of β-lactamase inhibitors and substrate profile of IRT-4 suggested that such an ionic bond was implicated in the alteration of the mechanistic **process** of TEM-1 β-lactamase.

L13 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:567887 CAPLUS
DOCUMENT NUMBER: 119:167887
TITLE: Polarographic determination of **aztreonam**
AUTHOR(S): Gonzalez Perez, C.; Gonzalez Martin, M. I.; Martinez Carabias, C.
CORPORATE SOURCE: Fac. Quim., Univ. Salamanca, Salamanca, 37008, Spain

SOURCE: Analytical Letters (1993), 26(8), 1649-55
CODEN: ANALBP; ISSN: 0003-2719
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The polarog. behavior of **aztreonam** is studied. In **acid** media, at pH values lower than 6, in differential pulse polarog. a peak is observed at a potential close to -0.6 V. The optimum conditions for the polarog. signal are established and the different parameters affecting the electrochem. **process** are studied. The relationship between peak intensity and the concentration of **aztreonam** is linear for concns. lower than 1.0 + 10-5 M, the detection limit being 1.4 + 10-8 M. The presence of l-arginine does not affect the polarog. signal of **aztreonam** to any significant extent.

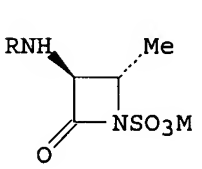
L13 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:51782 CAPLUS
DOCUMENT NUMBER: 118:51782
TITLE: Prediction and evaluation of penetration of drugs into cerebrospinal fluid in human
AUTHOR(S): Hamada, Jun; Sawada, Yasufumi; Nakamura, Kouichi; Yamada, Yasuhiko; Iga, Tatsuji
CORPORATE SOURCE: Dep. Pharm., Univ. Tokyo Hosp., Japan
SOURCE: Byoin Yakugaku (1992), 18(4), 349-60
CODEN: BYYADW; ISSN: 0389-9098
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The prediction of the distribution of highly lipophilic drugs into cerebrospinal fluid (CSF) was conducted by considering simple diffusion **process** and pH partition theory. CSF/plasma concentration ratio (CCSF/CP) was predicted from the fraction of unbound drug in plasma (fp), pKa, and pH of blood and CSF and compared with the observed CCSF/Cp values collected from literatures. In the case of highly-lipophilic drugs, the penetration into CSF could be predicted from various parameters as above. Since the penetration of more hydrophilic drugs into CSF could not be estimated from these parameters, we tried to predict CCSF/Cp values by using influx (PSI) rate constant from blood to brain and active efflux (kac) rate constant from brain to blood. The PSI value was water (Dm) based on Sawada's report (Y. Sawada et al., Am. J. Physiol., 258, H1585, 1990). The kac value was calculated on pharmacokinetic model considering the active efflux mechanism from brain to blood. A significant correlation (r = 0.96) between kac and PC of each drug was observed The predicted CCSF/Cp values based on this model was comparable with the observed values. These findings suggested that the CCSF/Cp values of lipophilic or hydrophilic drugs are predictable from various biochem., physicochem. and physiol. parameters.

L13 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:37491 CAPLUS
DOCUMENT NUMBER: 108:37491
TITLE: **Process** for the preparation of [3,4-(trans)]-3-acylamino-4-methyl-2-oxo-1-azetidinesulfonic **acid** derivatives and their pharmaceutically acceptable salts
INVENTOR(S): Perez-Aranda Ortega, Agustin; Herranz Herranz, Rosario; Arribas Mocoroa, Enrique; Fernandez Resa, Piedad; Conde Ruzafa, Santiago; Nieves Elvira, Rosa; Roncal Serra, Fernando; Fernandez Sousa-Faro, Jose Maria
PATENT ASSIGNEE(S): Antibioticos S. A., Spain
SOURCE: Span., 40 pp.

CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 549891	A1	19860401	ES 1985-549891	19851212

PRIORITY APPLN. INFO.: ES 1985-549891 19851212
GI



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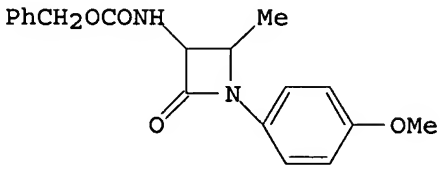

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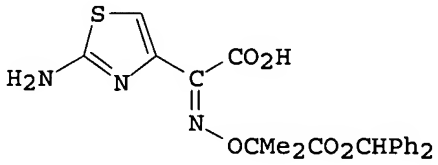

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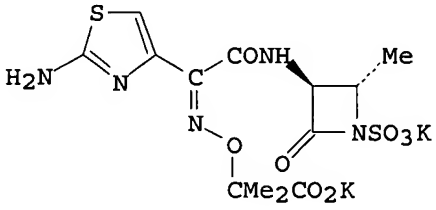


IV

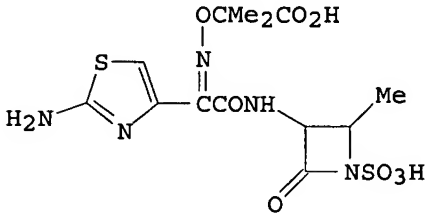
AB The antibiotic title compds. (I; R = H, acyl; M= H, alkali metal, quaternary ammonium) are prepared by a 9-step synthesis. For example, MeCOC(:NOH)CO2Et was reduced by Al amalgam and protected with PhCH2OCOCl to give MeCOCH(NHCO2CH2Ph)CO2Et, which was condensed with 4-H2NC6H4OMe and reduced with NaBH3CN/ZnCl2 to give 4-MeOC6H4NHCHMeCH(NHCO2CH2Ph)CO2Et. This was cyclized with PhMgBr (base) to give oxoazetidine derivative cis-II, which was epimerized by NaI/Me3SiCl/Et3N to give trans-II. The latter underwent N-deprotection with (NH4)2Ce(NO3)6, N-sulfonation with SO3-DMF complex in DMF, and hydrogenolysis over Pd/C to give I (R = M = H), which underwent amidation with thiazolylacetic **acid** derivative III in the presence of N-hydroxybenzotriazole and DCC, followed by deprotection with CF3CO2H/anisole and conversion, to give (thiazolylacetylamino)azetidinesul fonate salt IV (i.e., the racemic di-K salt of **aztreonam**).

L13 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:37488 CAPLUS
DOCUMENT NUMBER: 108:37488
TITLE: **Process** for the preparation of 2-[[[(2-amino-4-thiazolyl)[[2-methyl-4-oxo-1-sulfo-3-azetidinyl]carbamoyl]methylene]amino]oxy]-2-

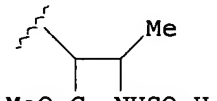
methylpropionic **acid**
INVENTOR(S): Montserrat Faba, Eusebio
PATENT ASSIGNEE(S): Inke S. A., Spain
SOURCE: Span., 8 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 545746	A1	19860116	ES 1985-545746	19850731

PRIORITY APPLN. INFO.: ES 1985-545746 19850731
GI



I



II

AB The title compound (I; i.e. the synthetic antibiotic **aztreonam**) is prepared by cyclization of the corresponding (sulfoamino)butanoate derivative II. A mixture of 10 mmol II in PhMe was refluxed for 24 h, followed by removal of solvent and 2 recrystns. from Et2O/EtOH, to give pure I in 71% yield.

L13 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:78228 CAPLUS
DOCUMENT NUMBER: 106:78228
TITLE: Comparison of antibiotic dosage regimens using pharmacokinetic and microbiologic factors
AUTHOR(S): Schumacher, Gerald E.
CORPORATE SOURCE: Coll. Pharm. Allied Health Prof., Northeastern Univ., Boston, MA, 02115, USA
SOURCE: Clinical Pharmacy (1987), 6(1), 59-68
CODEN: CPHADV; ISSN: 0278-2677
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A pharmacokinetic meta-anal. was performed for 33 antibiotics used in treating infections caused by microorganisms for which the antibiotics are considered to be agents of first choice or primary alternatives. The pharmacokinetic indexes assessed were the following components of the steady-state blood concentration-time profile: (1) the magnitude of the peak antibiotic serum concentration at steady state compared with the min. inhibitory concentration at steady state compared with the min. inhibitory concentration (CSSmax/MIC) and (2) the intensity index, a dimensionless term that reflects the contribution of the peak serum antibiotic concentration and the duration that this concentration is above the MIC. Substantial differences in CSSmax/MIC and intensity-index values were observed among antibiotics within an antibiotic class for individual microorganisms and for groups of microorganisms. Piperacillin [61477-96-1], amikacin [37517-28-5], and

tetracycline [60-54-8] showed the best mean performances of the ureido penicillins, aminoglycosides, and tetracyclines, resp. For the cephalosporins, cefadroxil [50370-12-2] displayed the highest mean values of the first-generation cephalosporins; cefuroxime [55268-75-2] and cefotetan [69712-56-7] showed the greatest measures for the second-generation agents; and all third-generation cephalosporins demonstrated very high mean performance indexes. Meta-anal. of pharmacokinetic performance factors is a useful technique for making intergroup and intragroup comparisons of antibiotics.

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L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:120849 CAPLUS
DOCUMENT NUMBER: 140:163626
TITLE: Preparation of **Aztreonam** via hydrolysis of tert-butyl **Aztreonam** with an aqueous **acid**
INVENTOR(S): Gyollai, Viktor; Meszaros Sos, Erzsebet; Szabo, Csaba; Singer, Claude; Salyi, Szabolcs
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceutical USA, Inc.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013133	A1	20040212	WO 2003-US24593	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063682	A1	20040401	US 2003-635659	20030805

PRIORITY APPLN. INFO.: US 2002-400699P P 20020805
US 2002-401749P P 20020808
OTHER SOURCE(S): CASREACT 140:163626
AB The invention relates to a **process** for the synthesis of **Aztreonam.** Specifically, the **process** entails hydrolyzing [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-tert-butoxycarbonyl-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid** (t-Bu **Aztreonam**) with an aqueous **mineral acid** to form **Aztreonam.**

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:259972 CAPLUS
DOCUMENT NUMBER: 132:293042
TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles

INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): General Mills, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021504	A1	20000420	WO 1999-US20905	19991006
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CA 2345815	AA	20000420	CA 1999-2345815	19991006
AU 9963872	A1	20000501	AU 1999-63872	19991006
EP 1119345	A1	20010801	EP 1999-951433	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527375	T2	20020827	JP 2000-575480	19991006

PRIORITY APPLN. INFO.:
US 1998-103700P P 19981009
US 1998-109696P P 19981124
US 1999-233443 A 19990120
WO 1999-US20905 W 19991006

AB A liquid encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liquid plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liquid plasticizer and the encapsulation of the active encapsulant is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous **process** to produce discrete, solid particles. The liquid content of the liquid encapsulant component provides substantially all or completely all of the liquid plasticizer needed to plasticize the matrix component to obtain a formable, extrudable, cuttable, mixture or dough. Removal of liquid plasticizer prior to extrusion is not needed to adjust the viscosity of the mixture for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform its intended function. Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l15 ibib abs hitstr tot

L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:120849 CAPLUS
DOCUMENT NUMBER: 140:163626

TITLE: Preparation of **Aztreonam** via hydrolysis of tert-butyl **Aztreonam** with an **aqueous acid**

INVENTOR(S): Gyollai, Viktor; Meszaros Sos, Erzsebet; Szabo, Csaba; Singer, Claude; Salyi, Szabolcs

PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceutical USA, Inc.

SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013133	A1	20040212	WO 2003-US24593	20030805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004063682	A1	20040401	US 2003-635659	20030805

PRIORITY APPLN. INFO.: US 2002-400699P P 20020805
US 2002-401749P P 20020808

OTHER SOURCE(S): CASREACT 140:163626

AB The invention relates to a **process** for the synthesis of **Aztreonam**. Specifically, the **process** entails hydrolyzing [3S-[3α(Z),4β]]-3-[[(2-amino-4-thiazolyl)[(1-tert-butoxycarbonyl-1-methylethoxy)imino]acetyl]amino]-4-methyl-2-oxo-1-azetidinesulfonic **acid** (t-Bu **Aztreonam**) with an **aqueous** mineral **acid** to form **Aztreonam**.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	195.45	351.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-31.19	-31.19

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